

THESIS

BOVINE TUBERCULOSIS SURVEILLANCE AT CATTLE ABATTOIRS IN IRELAND,

2008

Submitted by

Tulsi Ram Gompo

Department of Clinical Sciences

In partial fulfillment of the requirements

For the Degree of Master of Science

Colorado State University

Fort Collins, Colorado

Summer 2017

Master's Committee:

Advisor: Francisco Olea-Popelka

Sangeeta Rao
Marcella Henao-Tamayo

Copyright by Tulsi Ram Gampo 2017

All Rights Reserved

ABSTRACT

BOVINE TUBERCULOSIS SURVEILLANCE AT CATTLE ABATTOIRS IN IRELAND, 2008

Bovine tuberculosis (TB) surveillance is an ongoing program among abattoirs (slaughterhouses) in Ireland. It is a key complementary tool in addition to the tuberculin skin test to detect infected herds. A retrospective cross-sectional study was conducted to assess the association between potential risk factors and the risk of detection, and the subsequent risk of confirmation of bovine TB lesions for cattle slaughtered in 2008 in Irish abattoirs. Consequently, the abattoirs were ranked based on their efficiencies of detecting suspected bovine TB lesions and their subsequent confirmation in laboratory.

A database containing cattle records was obtained from the Center for Veterinary Epidemiology and Risk Analysis (CVERA) at University College Dublin, Ireland, that includes the results of animal movements, tuberculin test results, number of suspected bovine TB lesions detected during slaughter of animals and number of lesions confirmed as *Mycobacterium bovis* (*M. bovis*) in laboratory. The known potential risk factors impacting bovine TB lesions detection in Irish abattoirs were animal and herd level characteristics: age, sex, herd type, length of time a herd free from bovine TB after restriction, animal origin and District Electoral Division (DED) risk class. The data were analyzed to control for these potential risk factors when assessing the probability of detecting suspected bovine TB lesions among abattoirs in Ireland. Descriptive analysis was

performed to assess the distribution of cattle slaughtered over the different abattoir. Univariable logistic regression was applied to evaluate an association between the risk factors and detection of bovine TB lesions in the abattoirs. Multivariable logistic regression analysis was performed to calculate the adjusted risk of bovine TB lesion detection and confirmation for each abattoir.

During 2008, a total of 1,362,195 attested cattle were slaughtered in total thirty-five abattoirs in Ireland. Overall, 3,437 lesions (0.25%, or 25 per 10,000 slaughtered cattle) were detected, and from these, 2,187 (62.68%) bovine TB lesions were confirmed as caused by *M. bovis* in the laboratory. The crude detection risks varied from 0 to 56 lesions per 10,000 animals slaughtered. The average crude confirmation risks ranged from 0 to 100%. Ultimately, the abattoirs were ranked (1 being the best and 35 the worst) according to their effectiveness of bovine TB lesions detection and confirmation after adjusting the potential risk factors.

There is a considerable variability in efficiencies of Irish abattoirs in detecting and confirming bovine TB lesions. It is thus recommended that Irish abattoirs should be monitored regularly with regards their bovine TB slaughter surveillance effectiveness. Also, the abattoirs with lower than expected effectiveness should be strengthened in order to meet the required standards of the Irish bovine TB slaughter surveillance program.

ACKNOWLEDGMENTS

I am pleased to thank all the people who assisted during this research project. Firstly, I want to express my deep gratitude to my advisor Dr. Francisco Olea- Popelka for his continuous support and guidance throughout the research, analysis, and writing processes. I appreciate his subject matter knowledge in this field. He provided great insights into conducting research and writing a research paper on this topic.

Secondly, I want to thank Dr. Sangeeta Rao (departmental committee member) and Dr. Marcela Henao-Tamayo (interdepartmental committee member) for their suggestions and motivation for this project and manuscript writing.

I would also like to thank Dr. James O’Keeffe, Dr. Paul White, Guy McGrath, Dr. Simon More from the Department of Agriculture, Fisheries and Food, Dublin and University of College Dublin for their coordination in providing me the research data through the government of Ireland.

Last but not the least, I want to thank Fulbright Program, Department of State for sponsoring my MS program at Colorado State University.

DEDICATION

This thesis is dedicated to my parents who inspired me to be a veterinarian since childhood.

Thank you, Dad, for teaching me the basic tools of veterinary practice since my childhood and I am trying to walk in your footsteps.

Also, I want to dedicate this thesis to those people who lost their lives during the massive earthquake in Nepal of April 2015. May their souls rest in peace and may God give a power of endurance among the bereaved families.

TABLE OF CONTENTS

ABSTRACT	ii
ACKNOWLEDGMENTS	iv
DEDICATION	v
LIST OF TABLES	viii
LIST OF FIGURES	x
CHAPTER 1: LITERATURE REVIEW	1
1.1 Introduction.....	1
1.2 Mode of transmission of <i>Mycobacterium bovis</i>	2
1.3 Pathology of bovine tuberculosis in cattle	2
1.4 Control policy of Bovine TB	4
1.5 History of Bovine Tuberculosis and Cattle Trade in Ireland.....	5
1.6 Role of wildlife in the epidemiology of bovine tuberculosis in Ireland	6
1.7 Current Bovine TB control policy in Ireland.....	7
1.8 The Tuberculin skin test in Cattle in Ireland	8
1.9 Limitation of the Tuberculin test	10
1.10 The slaughter surveillance in Ireland	10
1.11 Potential Risk factors contributing to bovine TB lesions detection at slaughter.....	12
<i>Animal and herd level risk factors:</i>	13
1.12 Limitation of slaughter surveillance in Ireland	15
1.13 Laboratory components for the detection of bovine TB in Ireland.....	16
<i>Histopathology</i>	16
<i>Culture of M. bovis</i>	17
<i>Blood based test</i>	17
1.14 Thesis objectives:	18
CHAPTER 2: MATERIAL AND METHODS	19
2.1 Data sources:.....	19
2.2 Data Descriptions:	19
<i>Animal component</i>	21
<i>Tuberculin test</i>	21
<i>Abattoir component</i>	21
<i>Laboratory component</i>	22
2.3 Study Population:	22
2.4 Study Design:	22
2.5 Statistical Analysis:	23
2.6 Risk factors:	23
2.7 Descriptive analysis:	23
2.8 Univariable analysis:	24
2.9 Adjusted detection risk:	24
2.10 Adjusted Confirmation Risk:.....	25

CHAPTER 3: RESULTS	26
3.1 Descriptive analysis.....	26
<i>Crude ranking of abattoirs (slaughterhouses)</i>	26
<i>Age</i>	28
<i>Gender</i>	29
<i>Herd Type</i>	30
<i>Season</i>	30
<i>Animal Origin</i>	31
<i>Years Free</i>	32
<i>DED Risk Category</i>	33
3.2 Univariable logistic regression analysis:	33
<i>Age</i>	33
<i>Herd Type</i>	35
<i>Gender</i>	36
<i>Season</i>	37
<i>Animal Origin</i>	38
<i>Years Free</i>	38
<i>DED Risk Class</i>	39
3.3 Multivariable logistic regression analysis.....	41
<i>Age</i>	41
<i>Gender</i>	41
<i>Season</i>	41
<i>DED Risk Class</i>	42
<i>Years Free</i>	42
<i>Herd Type</i>	42
<i>Animal Origin</i>	43
3.4 Adjusted ranking of abattoirs (slaughterhouses)	45
CHAPTER 4: DISCUSSION.....	48
CHAPTER 5: CONCLUSION	53
REFERENCES	54

LIST OF TABLES

Table 1: Variables related to slaughter surveillance for year 2008 in Ireland.	20
Table 2: Crude risk and rank of abattoirs for bovine TB lesion detection in cattle slaughter in Ireland in year 2008.	27
Table 3: Distribution of suspected bovine TB lesions detected and confirmed as <i>M. bovis</i> among animals of different age categories in Irish abattoirs during 2008.	28
Table 4: Distribution of suspected bovine TB lesions detected and confirmed as <i>M. bovis</i> among female and male cattle in Irish abattoirs during 2008.	29
Table 5: Distribution of suspected bovine TB lesions detected and confirmed as <i>M. bovis</i> among animals of different herd types in Irish abattoirs during 2008.	30
Table 6: Distribution of suspected bovine lesion detected and confirmed as <i>M. bovis</i> among animals at different seasons in Irish abattoirs during 2008.	31
Table 7: Distribution of suspected bovine TB lesions detected and confirmed as <i>M. bovis</i> among purchased and homebred animals in Irish abattoirs during 2008.	32
Table 8: Distribution of suspected bovine TB lesions detected and confirmed as <i>M. bovis</i> among animals of different year free category in Irish abattoirs during 2008.	32
Table 9: Distributions of suspected bovine TB lesions detected and confirmed as <i>M. bovis</i> among animals slaughtered of different DED risk class in Irish abattoirs during 2008.	33
Table 10: Univariable analysis for the association between animal age and risk of suspected bovine TB lesion detection among animals slaughtered in Irish abattoirs during 2008.	34
Table 11: Univariable analysis for the association between animal age and risk of confirming bovine TB lesions in Irish abattoirs during 2008.	34
Table 12: Univariable analysis for the association between types of animal herd and risk of suspected bovine TB lesion detection among animals slaughtered in Irish abattoirs during 2008.	35
Table 13: Univariable analysis for the association between types of herds and risk of confirming bovine TB lesions in Irish abattoirs during 2008.	36
Table 14: Univariable analysis for the association between animal's gender and risk of suspected bovine TB lesion detection among animals slaughtered in Irish abattoirs during 2008.	36

Table 15: Univariable analysis for the association between gender of animals and risk of confirming bovine TB lesions in Irish abattoirs during 2008.....	36
Table 16: Univariable analysis for the association between seasons of the animals slaughtered and risk of suspected bovine TB lesion detection among total animals slaughtered in Irish abattoirs during 2008.....	37
Table 17: Univariable analysis for the association between the seasons of the animals slaughtered and risk of confirming bovine Tb lesions in Irish abattoirs during 2008.	37
Table 18: Univariable analysis for the association between the animal origin and risk of suspected bovine TB lesions detection among animals slaughtered in Irish abattoirs during 2008.....	38
Table 19: Univariable analysis for the association between the animal origin and risk of confirming bovine TB lesions in Irish abattoirs during 2008.....	38
Table 20: Univariable analysis for the association between the length of year free of herds from bovine TB and risk of suspected bovine TB lesions detections among animals slaughtered in Irish abattoirs during 2008.....	39
Table 21: Univariable analysis for the association between the length of year free of herds from bovine TB and risk of confirming bovine TB lesions in Irish abattoirs during 2008.....	39
Table 22: Univariable analysis for the association between the DED risk class and risk of suspected bovine TB lesion detections among animals slaughtered in Irish abattoirs during 2008.....	40
Table 23: Univariable analysis for the association between the DED risk class and risk of bovine TB lesion confirmations among animals slaughtered from attested herds in Irish abattoirs during 2008.....	40
Table 24: Number of animals slaughtered for each confounding variables, the percentage of detection, percentage of confirmation and adjusted ORs of detection and confirmation.	44
Table 25: The crude and adjusted risk of bovine TB lesions detection, and abattoir ranking (high to low), in Ireland during 2008.....	46
Table 26: The crude and adjusted risk of bovine TB lesions confirmation, and abattoir ranking (high to low), in Ireland during 2008.....	47

LIST OF FIGURES

Figure 1: The age distribution among the slaughtered animals.	29
--	----

CHAPTER 1: LITERATURE REVIEW

1.1 Introduction

Bovine tuberculosis (TB), caused by *Mycobacterium bovis* (*M. bovis*), is a zoonotic disease that affects cattle around the world (Collins, 2006). Moreover, the organism has broad host range including other livestock species, wildlife species, and humans (Michel et al., 2010). Domestic species susceptible to *M. bovis* are cattle, water buffalo, swine, sheep, llamas and deer (Hunter, 1996 ; Michel et al., 2010). Bovine TB has been documented throughout the world, including areas where livestock and wildlife interaction take place, and the infection has been documented between domestic and wildlife species. Susceptible wildlife species include white-tailed deer (*Odocoileus virginianus*) in the United States, European badgers (*Meles meles*) in Ireland and Britain, brush-tailed possums (*Trichosurus vulpecula*) in New Zealand, wild boar (*Sus scrofa*) in Europe, and African buffalo (*Syncerus caffer*) and antelope species in Africa (Michel, 2002; Drewe et al., 2014).

TB caused by *M. bovis* in humans is known as zoonotic TB (Olea-Popelka et al., 2017). The true burden of the zoonotic TB at a global scale is underestimated due to paucity of information among the public health officials regarding the importance of *M. bovis* in contribution of human TB. Lack of routine surveillance systems in low income countries and inadequate laboratory facilities to differentiate between *M. bovis* and *M. tuberculosis* in general (Cosivi et al., 1998 ; Thoen et al., 2010 ; Müller et al., 2013; Pérez-Lago et al., 2014; Olea-Popelka et al., 2017) are factors affecting the current knowledge of zoonotic TB in humans.

1.2 Mode of transmission of *Mycobacterium bovis*

The primary route of transmission for *M. bovis* among all species is respiratory, although other less common routes can include oral, congenital, or entry through open wounds (Doran et al., 2009; Good et al., 2011). In humans, *M. bovis* infections occur most commonly in the developing countries where there exist practices of drinking unpasteurized dairy products, occupational exposure to handling infected livestock and poor or no existence of regular testing programs for bovine TB in livestock system (Ayele et al., 2004). Also, the risk of transmission of bovine TB disease is higher in bovine TB endemic areas where people are more likely to be in direct contact with animals (such as farmers, veterinarians, abattoirs workers) (Olea-Popelka et al., 2017).

1.3 Pathology of bovine tuberculosis in cattle

M. bovis enters the body through aerosol route. Macrophages phagocytize *M. bovis*, which are eventually transported to lymph nodes by the lymphatic system. The macrophages laden with *M. bovis* attract T helper cells that subsequently destroy the infected macrophages. The killed macrophages debris from dead surrounding tissues creates caseous necrosis and forms a granuloma. The granuloma restricts the mycobacterium from infecting surrounding tissues, but also provides a niche for the bacteria to survive. Bovine TB manifests as chronic granulomatous caseous necrotizing lesions that mainly affect lungs and lymph nodes but also infects other organs. The infections remain covert for months or years until the functionality of an organ is completely impaired (Domingo et al., 2014).

The process of infection in cattle by *M. bovis* occurs as follows: primary infection occurs when the organism gains entry through the mucous membrane or alveolar spaces and the immune system responds to the bacterial cell wall and activates the inflammatory process for

phagocytosis. After phagocytosis by macrophages, the mycobacteria and neutrophils accumulate at the sites of infections (Arentz & Hawn, 2007). While in humans with a strong immunity, about 90% of infections are controlled through this initial immune response resulting in clearance of mycobacteria or control of infection for decades known as latent TB infection (LTBI). Only a few individuals progress to active tuberculosis (O'Garra et al., 2013). When the body's cell-mediated immune (CMI) response is not able to control inflammatory process the tissue damage continues until the primary granuloma becomes larger. This happens most frequently in the alveolar spaces. As the disease progresses, a typical gross lesion of TB forms known as tubercle, which contains an encapsulated connective tissue with central caseous necrosis. In lung tissue, the lesions can be extended into the bronchioles and bronchial tree. The ulcerative lesions later lead to formation of chronic organ TB (Domingo et al., 2014).

The TB organism, carried by the lymphatics, forms an initial primary complex in draining lymph node. The most common location is frequently found in the lower respiratory tract of animals. The organism spreads to different part of the body leading to generalization of the infection and this occurs via lymphatics or hematogenous dissemination of mycobacteria. The most common form of generalized infection is known as miliary TB, which involves many white-yellow necrotic foci similar to millet seeds. It usually occurs when the CMI wanes; some animals with miliary TB may be "anergic". They will not show any reaction to tuberculin or blood IFN- γ tests (Domingo et al., 2014).

1.4 Control policy of Bovine TB

Several countries have implemented official bovine TB control programs, which often consist of ‘test and slaughter’ approach to control the disease. Test and slaughter is composed of two main components: 1) testing of live animals using the tuberculin skin test, and 2) carcass inspection in abattoirs for detection of bovine TB lesions (Amanfu, 2006). The specific approaches and procedures in each country are largely dependent on the prevalence of the disease, the socio-economic capacities of the country and the epidemiological scenario. For example, in the USA, bovine TB eradication programs started in 1917 and are a joint venture of U.S. Department of Agriculture (USDA) Animal and Plant Inspection Services (APHIS), Food Safety and Inspection Services (FSIS), state health agencies and livestock producers (Kaneene et al., 2006).

Currently, slaughter surveillance is one of the important components to control bovine TB in USA. The program was first applied in the 1960s, when the prevalence of the bovine TB was low. The current bovine TB control program focuses on slaughter surveillance along with trace back investigations of infected herds (Humphrey et al., 2014).

In Europe, the EU Directive 64/432/EEC (European Commission, 1964) has classified European countries on the basis of bovine TB prevalence as Officially Tuberculosis Free Country (OTF) including Belgium, Germany, Netherlands, Poland, Switzerland, France and all others as non-Officially Tuberculosis Free Country (non-OTF). Both OTF and non-OTF European countries have slaughter surveillance implemented. In Great Britain, slaughter surveillance contributed in detecting 165 new TB incidents in the cattle herds as a whole; around 35% of incidents in non-bovine TB endemic areas where the routine field testing against bovine TB is done every four years (Shittu et al., 2013).

In developing countries like Cameroon, abattoirs are controlled by government. Usually they detect a more advanced stage of bovine TB infection. Previous prevalence studies identified that bovine TB cases were as low as 1% in Cameroon. The same studies, however, also suggest as high as 51% of the inspected lesions had the mycobacterial infections with detection of acid fast bacilli (Egbe et al., 2016). Similarly, in Ethiopia, a study conducted by Asseged et al. (2004) revealed that 1.5% of cattle in Addis Abba had TB lesions. This study, however, showed that routine abattoir inspection was only able to detect 55% of cattle with confirmed lesions.

1.5 History of Bovine Tuberculosis and Cattle Trade in Ireland

In Ireland, the national control program to eradicate bovine TB from cattle herds was started regionally in 1954 and was subsequently extended to whole country by 1962 (Good, 2006). With the introduction of the bovine TB eradication program, all herds were given an individual herd number and, an animal identification system was established subsequently in Ireland (Good, 2006). The bovine TB eradication program includes annual herd testing using single intradermal cervical comparative tuberculin test (SICCT), compensating farmers for slaughter of reactors, and controlling movement of cattle (Monaghan et al., 1994). In 1998, Eradication of Animal Diseases Board (ERAD) was established and a vigorous four-year project with a special check test for high-risk herds created. Subsequently, classification of the herds based on the disease incidence were undertaken to eradicate the disease in Ireland. After the implementation of this policy, the herd prevalence of bovine TB dropped to 0.5% from 17% in a decade (Griffin et al., 2005).

The rearing and trading of cattle and their products play a vital role in the gross economy of Ireland. Currently, the Irish national cattle herds are comprised of approximately 6.9 million

animals. Each year the country exports approximately 180,000 live cattle and 503,000 tons of beef worth €2.41 billion (DAFM, 2015). Ireland continues to implement a comprehensive disease control program and policy to ensure the viability of this portion of their economy (More et al., 2010).

1.6 Role of wildlife in the epidemiology of bovine tuberculosis in Ireland

The Eurasian badger (*Meles meles*) is considered a reservoir for *M. bovis* in Ireland (Murphy et al., 2010; Corner et al., 2011). Badgers are a nocturnal species, weighing 10-16 kg that are found around the cattle farms and pastureland. Badgers are adapted for digging and burrowing and live in social groups (Corner et al., 2011). It has been postulated that transmission of *M. bovis* to cattle can occur via direct contact with badgers or indirectly through excreta of badgers in grazing pastures and near cattle feed sources (Rogers et al., 2000). It is estimated that the indirect contacts with wildlife reservoirs are more significant than direct contacts in terms of disease transmission (Drewe et al., 2013).

A study by Byrne et al. (2015) in Ireland identified a positive association between a badger testing positive to *M. bovis* and cattle infection prevalence at spatial scale of 1 km around the badger's setts. Byrne et al. (2015) found that overall badger-level prevalence of *M. bovis* was 11.3% (95% CI:10.5-12.3) and sett-level prevalence of *M. bovis* infection was 15.2% (95% CI:14.0-16.4). One of the effective ways to reduce the prevalence of infections in badgers is by culling. Byrne's studies also found out a sharp decline in prevalence of *M. bovis* in badgers from 26% to 11% during their study from 2007 to 2013 in places where badgers were culled which shows that badgers are a potential risk factor in disease transmission.

The presence of a wildlife reservoir is an important constraint against the goal of eradicating bovine TB in Ireland, thus, controlling the disease in badger populations is a key aspect of controlling the disease in cattle. Studies of badger removal in four different areas of Ireland demonstrated that cattle and badgers shared the same *M. bovis* strains in a given geographical areas, suggesting the potential crossover of the disease between these species (Olea-Popelka et al., 2005; Sheridan, 2011). With agreement from the National Park and Wildlife Services, the Department of Agriculture Food and the Marine (DAFM) has set up a wildlife unit in Ireland, that focuses in controlling badger's densities where cattle had concurrent TB cases (Corner et al., 2012).

1.7 Current Bovine TB control policy in Ireland

The first step in the surveillance of bovine TB is screening of animals by a skin test known as Single Intradermal Comparative Cervical Test (SICCT). The sensitivity of SICTT has been reported to range between 70-90% (Monaghan et al., 1994) and the specificity is 99.98% (Goodchild et al., 2015). It is conducted through government veterinary inspectors and private veterinary practitioners each year. If cattle test positive (reactors), these animals are rapidly removed from the herd and slaughtered. The source herds of reactor animals are restricted from movement and retested. The restricted herds are lifted from restriction after all animals test negative on two consecutive tests at two months' interval (Monaghan et al., 1994; de la Rua-Domenech et al., 2006; Duignan et al., 2012).

Another important component of the bovine TB eradication program in Ireland is routine slaughter surveillance by veterinary inspectors, aimed at detecting gross lesions (tuberculous granulomas) suggestive of bovine TB during meat inspection at abattoirs. This is an important

component to identify infected animals/herds. Furthermore, the suspected lesions are submitted for laboratory confirmatory diagnosis of TB by microscopy, histology, and culture (Corner, 1994; Frankena et al., 2007; Olea-Popelka et al., 2012).

Currently, a field vaccination program for badgers using the Bacillus-Calmette Guerin (BCG) vaccine has been implemented. Aznar et al. (2011) showed that BCG vaccination can decrease disease severity in badgers. However, a modeling study has suggested that although there are significant benefits to vaccination, it is not able to break the transmission pathways completely (Aznar et al., 2011).

1.8 The Tuberculin skin test in Cattle in Ireland

The SICCT is one of the primary diagnostic tools approved by the Council Directive 64/432 (European Commission, 1964). It involves the simultaneous injection of both bovine and avian tuberculin in separate sites at the neck region in an animal. The interpretation is based on a principle that cattle infected with *M. bovis* shows greater skin reaction to bovine tuberculin than to avian tuberculin. Generally, infection with other tuberculosis strains shows the greater reaction to avian tuberculin injection areas (de la Rua-Domenech et al., 2006).

Immunology of the tuberculin test

When tuberculin, a purified protein derivative (PPD) from mycobacteria is intradermally injected, it produces a delayed-type hypersensitivity in animals (de la Rua-Domenech et al., 2006). The bovine tuberculin, currently used in European countries, is a derivative of a field strain of *M. bovis* AN5, while the avian tuberculin is obtained from cultures of specific strains of avian (*M. avium* ssp. *avium*) TB bacilli (Inwald et al., 2003). When an animal has earlier

exposure to the bacteria, the T-cells are sensitized and injecting tuberculin triggers an immune response which reaches maximum intensity around 72 hours post-injection (Pollock & Neill, 2002).

Test procedure:

An injection site in the cervical region of an animal is clipped and cleaned. The fold within each clipped skin area is measured and sites are marked prior to injection. The test is performed by injecting 0.1 ml each of *Mycobacterium avium*-derived protein and *M. bovis*-derived protein intradermally at two injection sites in the neck region. The 1 ml tuberculin syringe is used to inject the purified protein derivative. The distance between the two injections should be approximately 12–15 cm (OIE, 2015). The difference in the initial skin thickness after 72 hours is measured (Monaghan et al., 1994).

Test Interpretation:

When the bovine reaction is 4 mm greater than the avian reaction, or if local clinical signs such as edema, exudation, necrosis, or pain are present at the bovine injection site, an animal is considered a “standard reactor” (Green & Cornell, 2005). An animal is considered inconclusive to the test when the bovine reaction is between 1 to 4 mm greater than the avian reaction and there are no clinical signs at the bovine site. A negative result is recorded when no bovine reaction is present or when the bovine reaction is equal to or smaller than the avian reaction in the absence of clinical signs (Monaghan et al., 1994). According to Monaghan et al. (1994), the sensitivity of SICTT is estimated to be as high as 70-90%, thus, there is a probability of false negative reactors. A recent study by Goodchild et al. (2015) in Great Britain estimates test

specificity for non-infected herd as high as 99.983% (99.979 to 99.987%) when using a standard cut-off. These figures range depending upon the cut off criteria used like 99.915 % specific for a severe cut-off which includes severe and standard reactors and 99.871% for an ultra-severe cut-off, which includes inconclusive, severe and standard reactors. The herd-wise specificity was estimated to be about 99.5% (Goodchild et al., 2015).

1.9 Limitation of the Tuberculin test

The median sensitivity of SICCT is 75%, and thus, some infected animals go undetected when the tuberculin test is used as an screening test (Morrison et al., 2000). A false negative may result due to poor body condition of diseased animal, anergy, immunosuppression for other reasons, or desensitization due to pregnancy, lactation, or concurrent disease (de la Rua-Domenech et al., 2006). The SICCT used in Ireland and UK is considered a good herd test but a poor animal test because the herd level sensitivity (HSe) of SICCT is higher than the individual animal sensitivity. A herd is considered infected if at least one standard reactor is detected (Christensen & Gardner, 2000).

1.10 The slaughter surveillance in Ireland

According to Kaneene et al. (2006); Frankeena et al.(2007) and Olea-Popelka et al. (2012), slaughter surveillance is one of the key components in detecting infections in herds. The identification of bovine TB lesions during meat inspection is highly important for disease surveillance and control of infections, even in countries with officially TB-free (OTF) status (Domingo et al., 2014). The postmortem examinations of animals during the slaughter is not only a useful tool in detecting the infected herds missed by the skin testing (SICCT surveillance) but also one of the means of monitoring the efficiency of the skin testing (Pascual-Linaza et al.,

2016). The detection of lesions at abattoirs is a cost-effective measure for passive surveillance of bovine TB (Schiller et al., 2011). In Ireland, about 36% of bovine TB breakdowns between 1995 to 2010 were first detected by abattoir's surveillance (Abernethy et al., 2013). In more recent years (1999-2007), between 27 and 46% of all new herd breakdowns have been detected by this method (O'Keeffe and White, 1999 in Frankeena et al., 2007). Thus, slaughter surveillance is a complementary tool to tuberculin test applied in the Republic of Ireland.

Routine slaughter surveillance is based on palpation, incision, and the inspection of a defined range of lymph nodes. Because bovine TB lesions cannot generally be distinguished from non-tuberculous granulomas on gross inspection alone, suspect lesions from attested animals are sent to a diagnostic laboratory for confirmation (Frankeena et al., 2007; Olea-Popelka et al., 2012).

The routine ante- and post-mortem inspections of all cattle slaughtered in Irish abattoirs are usually carried out by private veterinarians on a part-time basis known as Temporary Veterinary Inspectors (TVI). These private veterinarians take two-week training courses on EU regulations and the correct postmortem practices before approval to act as TVIs (Duignan et al., 2012).

Despite the importance of abattoir surveillance, the isolation of bacteria from culture in a laboratory is the only definitive diagnosis for the confirmation of bovine TB (Corner, 1994). An animal is considered positive for bovine TB if lesion detected is positive by histopathology and/or culture in Ireland (Frankena et al., 2007; Olea-Popelka et al., 2012).

Two studies by Frankena et al. (2007) and Olea-Popelka et al. (2012) revealed that there was a great variation in effectiveness of detection of the bovine TB lesions among Irish abattoirs. The average submission (detection) risk for all the abattoirs was 22 per 10,000 animals, ranging from

0 to 58 per 10,000 in Frankena's (2007) study. Olea-Popelka et al. (2012) showed that an average submission risk of 25 lesions per 10,000 animals slaughtered ranging from 0 to 52.

1.11 Potential Risk factors contributing to bovine TB lesions detection at slaughter

The current bovine TB control program in Ireland has not achieved the eradication goal despite several control efforts, which may be due to several factors (More and Good, 2015). Firstly, bovine TB persistence either in herds or the locality contributes to residual infection among cattle. Secondly, an interaction of cattle herds with wildlife reservoirs such as badgers leads to reinfection of cattle herds. Thirdly, the detection of bovine TB lesions at abattoir is influenced by animal and herd level factors (Olea-Popelka et al., 2008; Berrian et al., 2012).

However, Morrison et al. (2000) hypothesized that the routine use of a screening test with imperfect sensitivity could result in a substantial pool of undetected infection in British cattle herd. Since reactors herds are restricted and retested after 60 day intervals, the use of more sensitive and multiple tests in parallel helps in reducing of the likelihood of re-infections and recurrent breakdowns in the herds (Goodchild & Clifton-Hadley, 2001).

Additionally, a previous history of bovine TB detection in the herds influences the risk of finding a bovine TB lesion at slaughter (Clegg et al., 2016). The risk of finding a case increases by about 1.5 times among cattle herds with a previous bovine TB history compared to herds without a previous bovine TB history. Similarly, the odds of finding a case increased with the time spent in the restricted herd. These findings of Clegg et al. (2016) are consistent with Olea-Popelka et al. (2008), who showed that the odds of the detecting a case increased with the number of standard reactors in the herds.

Further, Morrison et al. (2000) hypothesized that the routine use of a screening test with imperfect sensitivity could result in a substantial pool of undetected infection in the cattle herd. As the reactors herds are restricted and retested after 60 day intervals, the use of more sensitive and multiple tests in parallel helps in reducing the likelihood of re-infections and recurrent breakdowns in the herds (Goodchild & Clifton-Hadley, 2001).

Known risks factors that contribute to bovine TB lesion detection can be classified in the following categories.

Animal and herd level risk factors:

- a) Age: Age is one of the main risk factors for development of TB in cattle. As the development of TB takes a longer duration, older animals are more likely to detect lesions at abattoirs compared to younger animals. Age was found to be a potential risk factors for progression of disease in cattle of both developed and undeveloped countries (Olea-Popelka et al., 2008; Humblet et al., 2009). In Northern Ireland, there was an increase in the proportion of confirmed bovine TB with the increasing age, with animals > 6 years in age twice as likely to develop bovine TB than those younger than 2 years (Lahuerta-Marin et al., 2016).
- b) Sex: Sex is a risk factor that often related to management practices. For instance, a study in Tanzania showed that male oxen were more likely to have bovine TB than females, as males were kept for a longer period than females. In contrast, a cross-sectional study in Uganda revealed significantly more females with positive skin tests than males. This is due to difference in management practices in developing countries where the females are kept for calving and milking longer than males (Humblet et al., 2009).

- c) Season: In Ireland, the risk of testing positive on SICITT increased in winter months when animals are kept indoors. This is thought to be result of an increased stress due to greater stocking density when kept indoors (Lahuerta-Marin et al., 2016).
- d) Previous TB history in herds: Several studies have depicted that future risk of detecting bovine TB increases with previous herd history of testing positive for TB (Olea-Popelka et al., 2004 ; Wolfe et al., 2009; Clegg et al., 2013 ; Gallagher et al., 2013).
- e) Herd type: Suckler herds (that is, dams with beef-breed calves) are more likely to be detected with bovine TB compared to other herds (Clegg et al. 2016).
- f) District Electoral Divisions (DED) risk class: Animals from regions where the number of reactors are high, have a higher chance of having bovine TB lesions detected at the abattoirs (Frankena et al., 2007).
- g) Herd size: Herd size is an important risk factor. The risk of bovine TB increases with increasing herd size (Winkler & Mathews, 2015). Studies by Clegg et al. (2008, 2016), however, have found the opposite in Ireland. This could be because the initial studies were done at the herd level, whereas the Clegg et al. (2016) study was done at animal level. The management methods in Ireland, keeping animals in close contact with all other cattle on the farm in small herds, may increase the risk at animal level.
- h) Herd locations: Bovine TB risk is higher among contiguous herds located in areas with higher bovine TB prevalence (More and Good, 2015).
- i) Abattoirs: Abattoirs is also a potential factor for the detection and conformation of bovine TB lesions. There was a significant variation in finding bovine TB lesion among abattoirs and the subsequent confirmation of submitted lesion in the laboratory due to abattoir-related settings (Clegg et al., 2016; Frankena et al., 2007; Olea-Popelka et al., 2012).

1.12 Limitation of slaughter surveillance in Ireland

The visible lesions risk (VLR) is the number of animals deemed reactors at a herd test with a TB lesions detected at postmortem examination (Berrian et al., 2012). The visible lesion detection risk in recently tested animals is used as one of indicators of reliability of SICTT (Duignan et al., 2012). The VLR varies due to differences in physical settings, inspection facilities of the abattoirs, and experience and training of the veterinary inspector. Also, when disease prevalence falls, detection of lesions in reactor cattle is difficult (Frankena et al., 2007). Thus, a lesion detection in an abattoir is impacted in several ways. Firstly, it depends upon the size and location of the lesion. Smaller lesions are harder to detect if they are found in the lymph nodes. Pathological signs are hard to detect when the animal is at the early stage of infection and an exhaustive inspection procedure should be done to detect the incipient lesions (Corner, 1994). Secondly, the prevalence of disease from where cattle came to slaughter affects the detection and confirmation risk during slaughter (Corner, 1994). Thirdly, the detection of lesions can be complicated by several other diseases with similar clinical presentations, including actinomycosis ('lumpy jaw'), actinobacillosis ('wooden tongue'), coccidioidomycosis ('Valley fever'), paratuberculosis ('Johne's disease'), *Rhodococcus* spp. (in the form of a pyogranuloma), nocardiosis, neoplasms, parasitism, etc. (Ritacco et al., 2006).

In Ireland and United Kingdom (UK), 50-80 % of reactor cattle show no visible lesions (NVL) at slaughter and fail to have *M. bovis* isolated on culture (Goodchild & Clifton-Hadley, 2001; de la Rua-Domenech et al., 2006). The NVL and failure to isolate *M. bovis* could be the result of animals being in early stages of infection with *M. bovis*, when TB granulomas are small or infrequently seen during routine post-mortem examination (Goodchild & Clifton-Hadley, 2001).

Other possible causes would be disease latency and cross-reaction of antibodies against environmental mycobacteria with bovine tuberculin (Pollock & Neill, 2002).

Finally, many studies revealed that cases of the bovine TB persistence in Irish cattle herds may be due to residual infections among herds, environmental sources such as wildlife reservoirs, between-farm transmission, or introduction of infected cattle in disease free herds (More & Good, 2015). Ireland had one of the highest herd level prevalence of bovine TB in Europe (4.37%), in spite of its national control programs (European Food Safety Authority (EFSA), 2009; Schiller et al., 2011).

1.13 Laboratory components for the detection of bovine TB in Ireland

Histopathology

About 85% of diagnoses are based on histopathological examination of lesions submitted to the national bovine TB reference laboratory known as DAFM Central Veterinary Research Laboratory (CVRL). The results of the histopathology are highly correlated to the culture. The laboratory and the abattoirs in Ireland are linked to the AHCS, so the status of a given sample can be monitored easily (Duignan et al., 2012).

On the basis of histopathology, granulomatous lesions are classified into four types (Wangoo et al., 2005). Type I granulomas consist of clusters of epithelioid macrophages with multinucleated Langerhans-type cells and a thin rim of lymphocytes, and no necrosis. In type II granulomas, epithelioid macrophages, multinucleated Langerhans-type cells, and lymphocytes are more numerous, and caseous necrosis starts to develop in the centers of the tubercles. In type III granulomas, caseous necrosis is well developed, but mineralization is minimal. Type IV

granulomas are matured and have caseous necrosis with mineralization and development of fibrous encapsulations. Determining the type of granuloma helps in identification of the stage of disease and differentiating normal granulomas from those induced by vaccination and immunosuppression.

The procedure for analyzing the tissue via histopathology is as follows: the tissue from the granulomas are ground finely into small pieces and treated for non-mycobacteria. Next, they are concentrated by centrifugation and applied on microscopic slides and stained with the Ziehl-Neelsen stain for visualization. A positive smear shows short pink rods of TB bacilli (OIE, 2015).

Culture of M. bovis

M. bovis are non-motile rod-shaped bacteria with a mycolic acid cell wall (Corner et al., 2011). For primary isolation, tissue sediment is inoculated in Stonebrink's or Lowenstein medium that contains pyruvate or pyruvate and glycerol. The plates are incubated for 8 weeks at 37° C without CO₂. In a suitable pyruvate-based solid medium, colonies of *M. bovis* are smooth and off-white (buff) in color (OIE, 2015). Isolation of *M. bovis* must be carried out in at least a biosafety level (BSL) 2 laboratory due to its hazardous nature (Corner et al., 2012).

Blood based test.

Despite SICCT as the primary diagnostic test, a number of ancillary tests have been developed to improve the overall sensitivity and the specificity of bovine TB tests. The interferon gamma assay is an ancillary test that has improved sensitivity. It has been used in clearing infected herds and ensuring that fewer infected herds are missed at detection.

The interferon gamma assay (IFN- γ) is based on the cytokines produced by T-lymphocytes of bovine TB infected animals after stimulation using the *M. bovis* antigen. The IFN- γ test is more sensitive than SICCT, and has similar specificity (Menin et al., 2013). A study conducted in Spain has shown that the sensitivity of IFN- γ was as high as 89.3% (95% CI 77.5–97.2) (Alvarez et al., 2012). The IFN- γ test detects a substantial proportion of animals that escaped the tuberculin test because IFN- γ identifies animals at an earlier stage of disease than the skin test (Goodchild et al., 2003 ; Pollock et al., 2006).

1.14 Thesis objectives:

The objectives of this study are twofold:

- a) To evaluate the effectiveness of Irish abattoirs in detecting/confirming bovine TB lesions.
- b) To rank abattoirs based on bovine TB detection and confirmation risk, controlling (adjusting) for factors known to impact bovine TB lesion detection and confirmation in Ireland.

CHAPTER 2: MATERIAL AND METHODS

2.1 Data sources:

The data were obtained from the Department of Food and the Marine (DAFM), Republic of Ireland and The Centre for Veterinary Epidemiology and the Risk Analysis (CVERA) at University College, Dublin, Ireland. Three different data sources were used for this analysis:

- a) The Animal Health Computer System (AHCS), with tuberculin testing data of all herds in Ireland including all bovine TB reactor animals since 1989.
- b) The Cattle Movement and Monitoring System (CMMS), a fully operational animal identification system recording calf registrations, cattle movements (farm-to-farm, via a market and to slaughter plant) and on-farm deaths in Ireland since January 1, 2000.
- c) A laboratory database containing testing results (histopathology and culture reports since 2000) from the national slaughter plant surveillance program.

2.2 Data Descriptions:

The original surveillance data includes a total of 1,552,827 observations and 22 variables. These variables gave overview of the slaughter surveillance data keeping, though not all the variables were needed for this analysis. The following table is a description of the information contained in each variable that portrays different components of abattoir surveillance of Ireland.

Table 1: Variables related to slaughter surveillance for year 2008 in Ireland.

Variables	Descriptions
animal_id	Encoded tag no. of slaughtered animal
tb_skin_status	Recent skin test status, coded as follows: N = Negative/Clear; I= Inconclusive within previous 90 days; P=Test Positive (reactor).
abattoir_lesion_status	Abattoir lesion status coded as follows: N= No visible lesion(s); I=Abattoir lesion inconclusive; P= Abattoir lesion positive, C= Clear herd.
kill_herd_no	Encoded herd no. of kill herd.
kill_date	Date of slaughter of animal.
kill_type	The method of killing. S= Slaughter.
Kill_herd_no	The herd no of the slaughtered herd
abattoir_no	Original abattoir identity
birth_date	Birthdate of animals (form year 1998 onwards for this study).
birth_herd_no	Encoded birth herd no of animal during birth
gender	Male / female
date_purchase	Date of purchase of slaughtered animals (non-homebred animals only)
last_test_date	Date of last test in slaughtering herd prior to animal's slaughtered date.
first_herd_test_date	First recorded herd test date in slaughtering herd since 1989.
last_cl_date	Date of last clearance test in slaughter herd prior to animal's kill_date
within_epi	Were the animals obtained from the District Electoral Division (DED) risk area (Yes/No)?
restr_date	Date of restriction of slaughter herd where within epi = Y.
herd_type	DAI = Dairy; SUC= Suckler; BEE=Beef; OTH=Other.
kday	The day of killing of animal in "Day Month Year"
kyera	Kill year (2008)
age	The age of animals
year_clear	The time interval of the animals cleared from TB after restrictions (in years) to slaughter day
lesions	Detection of lesion. Presence=1 and absence=0.
confirmed	Confirmation of lesions. Positive=1, Negative=0

The variables are broadly classified on the following components:

Animal component

The variables contain information regarding animal and herd characteristics including age, gender, herd type, date of purchase, interval of herd TB clearance, tuberculin status and the geographical locations of animals brought for slaughter. The total number of attested cattle (i.e., negative to the SICTT test) that were sent to slaughter in Irish factories (abattoirs) during the year 2008 is 1,552,827.

Tuberculin test

The results of all the cattle with the tuberculin test are available since 1990. All herds in Ireland are tested at least once a year but the infected herds are tested more often. The database has the information of all the herds' identification number, location of the herd in each District Electoral Division (DED), the testing dates, and the total number of animals tested negative to tuberculin test. The data of tuberculin test data are used to calculate the animal level prevalence of bovine TB for the herds located in each District Electoral Division.

Abattoir component

There were 35 Irish abattoirs (slaughterhouses) operating in Ireland in 2008. Information on the abattoir includes abattoir number, total number of animals slaughtered, and the number of bovine TB lesions detected from each abattoir.

Laboratory component

Bovine TB suspected lesions are submitted to a laboratory for histopathology and bacteriology (culture) for *M. bovis* confirmation. The laboratory data include results indicating if bovine TB lesions were positive, negative and/or inconclusive to *M. bovis*.

2.3 Study Population:

Out of the total 1,552,827 attested cattle slaughtered in Irish abattoirs only 1,362,195 animals were included in this analysis after excluding those not matching our study criteria or having missing data. The inclusion and the exclusion criteria are listed as follows.

Exclusion Criteria: First, any animals with inconclusive results to skin test were not included in our study. There are 866 animals excluded from total slaughtered cattle due to inconclusive skin test. Next, all the animals belonging to a herd undergoing a TB episode prior to slaughter were excluded from the study. There are 189,993 animals having TB episodes prior to slaughter that were excluded from this study. Also, animal with incomplete data or the missing information on birthdates, year of clearance and gender were excluded from our study.

Inclusion Criteria: All the attested cattle (tested negative to the SICCT) with the complete data on potential confounding variables were included in the study, summing a total of 1,362,195 animals.

2.4 Study Design: This is a retrospective cross-sectional study to evaluate factors associated with the risk of detecting and confirming a bovine TB lesion among animals slaughtered in Ireland during 2008.

2.5 Statistical Analysis:

StataIC 14.2® (StataCorp, Lakeway Drive, College Station, TX, USA) was used for data cleaning, formatting, and statistical analyses.

2.6 Risk factors:

The risk factors selected for this analysis are based on the knowledge obtained from prior studies conducted by Frankeena et al. (2007) and Olea_Popelka et al. (2012) in Ireland. The factors selected for the study are the abattoirs, age and gender of the animals, the types of animal herds, season of the animal slaughtered, either purchased or home bred animals (animal origin), length of time a herd free from bovine TB after restriction, District Electoral Division (DED) of animal originated from. Thus, the final study model includes the data on eight potential confounding factors.

2.7 Descriptive analysis:

A descriptive analysis was conducted to calculate the crude risk of bovine TB lesion detection/confirmation for each abattoir. Abattoirs were ranked from highest to lowest bases on the risk (%) of detecting/confirming bovine TB lesions. Additionally, the crude risk was calculated for different animal and herd level factors. The frequency and distributions of confounding factors for each animal was also described in detail. The risk of detection and the confirmation were calculated for each abattoir and different factors using the following formula:

- i) Detection Risk =
$$\frac{\text{number of animals with bovine TB lesions detected}}{\text{number of animals slaughtered}}$$
- ii) Confirmation Risk =
$$\frac{\text{number of bovine TB lesions confirmed with } M. bovis}{\text{number of bovine TB lesions detected}}$$

The term detection risk is used interchangeably with the submission risk that was used with the similar previous studies.

2.8 Univariable analysis: Univariable logistic regression analysis was done to evaluate associations between each factor and the outcome (detection of bovine TB lesion in abattoirs and subsequent confirmation). The odds of detection and confirmation of lesions for each risk factor were calculated by this method.

2.9 Adjusted detection risk:

A multivariate logistic regression model was conducted to adjust the abattoirs ranking (risk of bovine TB lesions detection/submission) by adjusting results by the potential confounding effect of different animal and herd level factors known to be associated with bovine TB in Ireland.

The following multivariable logistic regression model was utilized for this study:

$$\text{Logit} (P[Y=1|F+x]) = \mu + F + x_1 + x_2 + x_3 + \dots + x_7,$$

where $(P[Y = 1|F + x])$ is the probability that a lesion detection among animals slaughtered at each abattoir while adjusting for a set of confounders (x); μ is the overall mean; and “F” denotes all the 35 Irish factories operating in 2008 where the attested animals were slaughtered. Abattoir (F) is our main risk factors and the covariates are (x_n) where,

x_1 = Age of animal

x_2 = Gender of animals with two categories: Male (M) and Female (F)

x_3 = Herd type with four factor categories: Beef (B), Dairy (D), Suckler (S), and Others (O).

x_4 = Length of time animal free from TB after restriction.

x_5 = DED risk (four classes: 1=very low, 2=low, 3=medium and 4=high).

x_6 = Seasons of animals slaughtered (four classes: Jan-Mar, Apr-Jun, Jul-Sep, and Oct-Dec).

x_7 = Animal origin (Homebred and purchased cattle)

The predicted probability of detecting a bovine TB lesions (%) based on these set of animal and herd level factors included in the model were obtained for each abattoir and used to calculate the adjusted ranking.

2.10 Adjusted Confirmation Risk:

A comparable multivariable logistic regression model as described in 2.9 was used to calculate the adjusted confirmation risk accounting for all the potential confounders. The adjusted confirmation risk for the lesion submitted to laboratory for each of the abattoir was calculated.

CHAPTER 3: RESULTS

3.1 Descriptive analysis:

Crude ranking of abattoirs (slaughterhouses):

There was a wide range of variation between the crude detection risks of suspected bovine TB lesions among all thirty-five abattoirs in Ireland (Table 2). The crude detection risk of the suspected bovine TB lesions among the abattoirs ranges from 0 to 0.56% (0 to 56 per 10,000 animals slaughtered) (Table 2) with an average of 25 per 10,000 animals slaughtered. The abattoirs were ranked from 1 to 33 (1 being the best abattoir and 33 being the worst) based on the crude detection risk.

Table 2: Crude risk and rank of abattoirs for bovine TB lesion detection in cattle slaughter in Ireland in year 2008.

Abattoir No	Number Slaughtered	Lesions Detected	Crude Detection	
			Risk (%)	Rank
1	72,238	184	0.25	11
2	53,409	91	0.17	24
3	60,007	137	0.23	17
4	78,932	84	0.11	30
5	57,711	189	0.33	6
6	57,555	80	0.14	26
7	53,278	158	0.30	9
8	59,533	72	0.12	27
9	58,179	176	0.30	8
10	72,194	383	0.53	2
11	46,334	93	0.20	20
12	54,986	129	0.23	16
13	2,438	6	0.25	14
14	39,041	94	0.24	15
15	52,528	100	0.19	21
16	54,117	90	0.17	25
17	71,482	397	0.56	1
18	4,766	10	0.21	19
19	52,210	158	0.30	7
20	50,015	216	0.43	4
21	9,772	8	0.08	31
22	39,612	47	0.12	28
23	58	0	0.00	33
24	47,408	1	0.00	32
25	50,292	91	0.18	22
26	27,935	111	0.40	5
27	22,263	63	0.28	10
28	39,233	203	0.52	3
29	17,617	37	0.21	18
30	1,108	2	0.18	23
31	667	0	0.00	33
32	41,456	0	0.00	33
33	5,399	6	0.11	29
34	3,155	8	0.25	12
35	5,267	13	0.25	13
Total	1,362,195		Average: 0.25	

Age:

Among the total 1,362,195 attested animals slaughtered used for this analysis, 48.3% of them were two to three years of age, 24.4 % of them were one to two years of age and more than 6% of animals were greater than 10 years old. The animal's age and the risk of suspected bovine TB lesion detection and its subsequent confirmation are shown in Table 3. The mean and median age distributions of the animals were 3.2 and 2.4 respectively (Figure 1). The risk of detecting and confirming suspected bovine TB lesion was found to increase with age.

Table 3: Distribution of suspected bovine TB lesions detected and confirmed as *M. bovis* among animals of different age categories in Irish abattoirs during 2008.

Age in (years)	Total Animals Slaughtered	Percent among age category	Number lesions detected	Bovine TB Detection risk (%)	Number lesions confirmed	Bovine TB Confirmation risk (%)
0-1	4,742	0.35	6	0.13	4	66.67
1-2	332,673	24.42	518	0.16	301	58.11
2-3	658,425	48.34	1,319	0.20	734	55.65
3-4	107,067	7.86	382	0.36	216	56.54
4-5	37,412	2.75	130	0.35	94	72.31
5-6	31,047	2.28	115	0.37	81	70.43
6-7	29,198	2.14	123	0.42	87	70.73
7-8	28,419	2.09	123	0.43	100	81.30
8-9	25,579	1.88	131	0.51	102	77.86
9-10	22,952	1.68	118	0.51	89	75.42
>10	84,681	6.22	472	0.56	379	80.30
Total	1,362,195	100	3,437	0.25	2,187	63.63

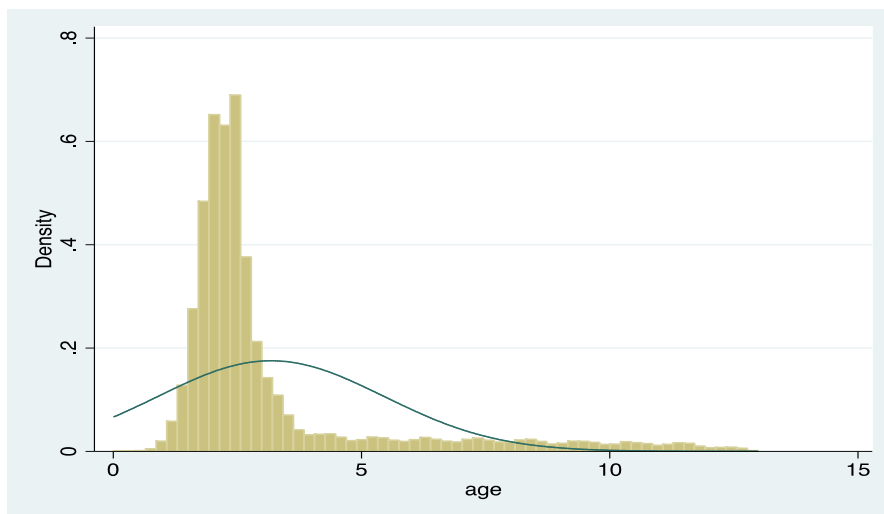


Figure 1: The age distribution among the slaughtered animals.

Gender:

Among the 1,362,195 attested animals slaughtered, 46 % of them were female and 54% were male. The risk of suspected bovine TB lesions detection and their confirmation was higher among females than males. The animal's gender distributions and risk of suspected bovine TB lesions detection and their subsequent confirmations are shown in Table 4.

Table 4: Distribution of suspected bovine TB lesions detected and confirmed as *M. bovis* among female and male cattle in Irish abattoirs during 2008.

Gender	Total animals slaughtered	Percent among gender	Number lesions detected	Detection risk (%)	Number lesions confirmed	Confirmation risk (%)
Female	623,398	45.76	1,835	0.29	1313	71.55
Male	738,782	54.24	1,602	0.22	874	54.56
Total	1,362,180	100	3,437	0.25	2187	63.63

Herd Type:

Out of total animals slaughtered, 40% of the animals were slaughtered from sucklers herd, 31% were from beef herds, 27% were from the dairy herd and 2% were from others herd category.

The risk of suspected bovine TB lesion detection was highest among sucklers and other breed types (on average 31 lesions per 10,000 animals slaughter) and lowest in dairy type (on average 18 per 10,000 animals slaughtered). On the other hand, the risk of suspected bovine TB lesions confirmation was higher among sucklers than other breed types, 69.5% and 61.7%, respectively.

The herd type distributions and risk of suspected bovine TB lesions detection and their subsequent confirmations are shown in Table 5.

Table 5: Distribution of suspected bovine TB lesions detected and confirmed as *M. bovis* among animals of different herd types in Irish abattoirs during 2008.

Herd Type	Total animals slaughtered	Percent among herd types	Number lesions detected	Detection risk (%)	Number lesions confirmed	Confirmation risk (%)
Beef	420,855	31.48	1,066	0.25	611	57.32
Dairy	359,627	26.9	639	0.18	382	59.78
Others	22,168	1.66	68	0.31	42	61.76
Suckler	534,112	39.96	1,630	0.31	1132	69.45
Total	1,336,762	100	3,403	0.25	2167	63.68

Season:

The risk of the suspected bovine TB lesions detected among animals varied with season. The risk of suspected bovine TB lesion detection was highest in autumn (0.29%) followed by summer (0.26%). Spring and winter have equal risk of bovine TB lesions detection among the slaughtered animals (0.23%). Also, the risk of lesions confirmations is highest during the summer and autumn (65% and 66.5 %) respectively with the overall risk of confirmations

63.63%. The seasonal distributions and risk of suspected bovine TB lesion detection and their subsequent confirmation are illustrated by Table 6.

Table 6: Distribution of suspected bovine lesion detected and confirmed as *M. bovis* among animals at different seasons in Irish abattoirs during 2008.

Season	Total animals slaughtered	Percent among seasons	Number lesions detected	Risk of detection (%)	Number Lesions Confirmed	Risk of Confirmation (%)
Jan-Mar	329,340	24.18	771	0.23	474	61.48
Apr-Jun	320,096	23.5	722	0.23	435	60.25
July-Sep	364,747	26.78	943	0.26	612	64.90
Oct-Dec	348,012	25.55	1,001	0.29	666	66.53
Total	1,362,195	100	3,437	0.25	2187	63.63

Animal Origin:

More than two third of slaughtered animals in 2008 were purchased cattle. Importantly, the risk of suspected bovine TB lesion detection among the purchased animals was higher than the homebred animals (on average 26 lesions per 10,000 animals and on average 20 lesions per 10,000 animals respectively). However, the risk of confirmation out of total lesions detected were 62.4% for purchased cattle and 62.1% for homebred cattle. The overall confirmation risk is 62.34 %.

The origin of animals and risk of suspected bovine TB lesions detection and their subsequent confirmations are illustrated in Table 7.

Table 7: Distribution of suspected bovine TB lesions detected and confirmed as *M. bovis* among purchased and homebred animals in Irish abattoirs during 2008.

Animal origin	Total animal slaughtered	Percent slaughtered	Number lesions detected	Detection risk (%)	Number lesions confirmed	Confirmation risk (%)
Purchased	917,138	70.82	2,402	0.26	1,499	62.41
Homebred	377,972	29.18	774	0.20	481	62.14
Total	1,295,110	100	3,176	0.25	1980	62.34

Years Free:

When the herds are tested positive for bovine TB, they are restricted for a certain time interval until they are tested negative in retesting. The time period after the herds are cleared from bovine TB restrictions to the time of slaughtered is defined as years free. The risk of suspected bovine TB lesion detection and risk confirmation decreases with the increase in the interval of the year free of bovine TB are illustrated in Table 8.

Table 8: Distribution of suspected bovine TB lesions detected and confirmed as *M. bovis* among animals of different year free category in Irish abattoirs during 2008.

Year free	Total animals slaughtered	Percent slaughtered	Number lesions detected	Number lesions Confirmed	Detection risk (%)	Confirmation risk (%)
0-1	276,735	20.7	796	523	0.29	65.70
1-2	147,476	11.03	395	264	0.27	66.84
2-3	111,339	8.33	292	191	0.26	65.41
3-4	80,431	6.02	205	120	0.25	58.54
>4	720,867	53.92	1,715	1,069	0.24	62.33
Total	1,336,848	100	3,403	2,167	0.25	63.68

DED Risk Category:

In Ireland, District Electoral Division (DED) is low-level territorial division. It is useful in locating the animal herds and in our analysis DED's were divided in four categories using quartiles based on prevalence of bovine TB that area (1=very low, 2=low, 3=medium and 4=High) based on the annual disease prevalence. The animal's DED risk class and the risk of suspected bovine lesion detection and confirmation are shown in Table 9.

Table 9: Distributions of suspected bovine TB lesions detected and confirmed as *M. bovis* among animals slaughtered of different DED risk class in Irish abattoirs during 2008.

DED Risk Class	Total animal slaughtered	Number lesions detected	Detection risk (%)	Number lesions confirmed	Confirmation risk (%)
Very Low	334747	748	0.22	425	56.82
Low	333486	763	0.23	457	59.90
Medium	337129	824	0.24	534	64.81
High	356833	1102	0.31	771	69.96
Total	1362195	3437	0.25	2187	63.63

3.2 Univariable logistic regression analysis:

Age: The odds of detecting suspected bovine TB lesions among slaughtered animals increased with age as shown in Table 10. Although the odds of detecting suspected bovine TB lesions were higher for animals of ages between 1-2 and 2-3 years of age compared to animals younger than a year old, these results were not statistically significant ($p=0.61$ and $p=0.26$, respectively).

However, there were statistically significant differences in detecting suspected bovine TB lesions among animals in all categories greater than three years of age when compared to animals younger than a year old.

Table 10: Univariable analysis for the association between animal age and risk of suspected bovine TB lesion detection among animals slaughtered in Irish abattoirs during 2008.

Age Category (years)	Odd Ratio (95% CI)	P-Value
0-1	Reference	-
1-2	1.2 (0.6-2.8)	0.61
2-3	1.6 (0.7-3.5)	0.26
3-4	2.8 (1.3-6.3)	0.01
4-5	2.8 (1.2-6.2)	0.02
5-6	2.9 (1.3-6.7)	0.01
6-7	3.3 (1.5-7.6)	<0.001
7-8	3.4 (1.5-7.8)	<0.001
8-9	4.1 (1.8-9.2)	<0.001
9-10	4.1 (1.8-9.3)	<0.001
>10	4.4 (2-9.9)	<0.001

The odds of the confirming suspected bovine TB lesions increased with the animal's age, however these results were not statistically significant (Table 11).

Table 11: Univariable analysis for the association between animal age and risk of confirming bovine TB lesions in Irish abattoirs during 2008.

Age Category(years)	Odd Ratio of confirmation (95% CI)	P-Value
0-1	Reference	-
1-2	0.7 (0.1-3.8)	0.67
2-3	0.6 (0.1-3.4)	0.59
3-4	0.7 (0.1-3.6)	0.62
4-5	1.3 (0.2-7.4)	0.76
5-6	1.2 (0.2-6.8)	0.84
6-7	1.2 (0.2-6.9)	0.83
7-8	2.2 (0.4-12.6)	0.39
8-9	1.8 (0.3-10.1)	0.53
9-10	1.5 (0.3-8.8)	0.63
>10	2.0 (0.4-11.3)	0.42

Herd Type:

The odds of the detecting suspected bovine TB lesions among the slaughtered animals varied with herd types as illustrated in Table 12. The odds of detecting bovine TB lesions were significantly higher among suckler herd (OR=1.2, 95% CI: 1.1-1.3, $p<0.001$) compared to beef herd. However, the odds of detecting bovine TB lesions were higher among other animals (OR=1.2, 95% CI: 0.9-1.5, $p=0.13$) compared to beef type but the result was not statistically significant. Animals from dairy herds had lower odds of disclosing bovine TB lesions when compared to animals from beef herds (OR=0.7, 95% CI: 0.6-0.8, $p<0.001$).

Table 12: Univariable analysis for the association between types of animal herd and risk of suspected bovine TB lesion detection among animals slaughtered in Irish abattoirs during 2008.

Herd Types	Odds Ratio (95% CI)	P Value
Beef	Reference	-
Dairy	0.7 (0.6-0.8)	<0.001
Others	1.2 (0.9-1.5)	0.13
Suckler	1.2 (1.1-1.3)	<0.001

Next, the odds of confirming bovine TB lesions among the suspected bovine TB lesions varied with herd types. The odds of confirming the suspected bovine TB lesions were higher among the dairy (OR=1.1, 95% CI: 0.9-1.4, $p=0.32$) and others (OR=1.2, 95% CI: 0.7-2.0, $p=0.47$) in comparison to beef herds, however these results were not statistically significant. While, the suckler herds (OR=1.7, 95% CI: 1.4-2.0, $p<0.001$) have significantly higher odds of confirming the suspected bovine TB lesions compared to beef herds in comparison to beef herds as shown in Table 13.

Table 13: Univariable analysis for the association between types of herds and risk of confirming bovine TB lesions in Irish abattoirs during 2008.

Herd Type	Odds Ratio (95% CI)	P Value
Beef	Reference	-
Dairy	1.1 (0.9-1.4)	0.32
Others	1.2 (0.7-2.0)	0.47
Suckler	1.7 (1.4-2.0)	<0.001

Gender:

The odds of detecting bovine TB lesions among females (OR=1.4, 95% CI: 1.3-1.5, $p<0.001$), is significantly higher than male animals as shown in Table 14.

Table 14: Univariable analysis for the association between animal's gender and risk of suspected bovine TB lesion detection among animals slaughtered in Irish abattoirs during 2008.

Gender	Odds Ratio (95% CI)	P Value
Male	Reference	-
Female	1.4 (1.3-1.5)	<0.001

Next, the odds of the confirming bovine TB among the lesions detected was twice as high in female (OR: 2.1, 95%CI: 1.8-2.4, $p<0.001$) compared to males and statistically significant as shown in Table 15.

Table 15: Univariable analysis for the association between gender of animals and risk of confirming bovine TB lesions in Irish abattoirs during 2008.

Gender	Odds Ratio (95% CI)	P Value
Male	Reference	.
Female	2.1 (1.8-2.4)	<0.001

Season:

The odds of detecting bovine TB lesions among animals slaughtered in summer (OR=1.1, 95% CI: 1-1.2, $p<0.04$) and autumn (OR=1.23, 95% CI: 1.1-1.4, $p<0.04$) were higher when compared to animals slaughtered in winter and the result were statistically significant as shown in Table 16.

Table 16: Univariable analysis for the association between seasons of the animals slaughtered and risk of suspected bovine TB lesion detection among total animals slaughtered in Irish abattoirs during 2008.

Season	Odds Ratio (95% CI)	P Value
Winter	Reference	-
Spring	0.96 (0.9-1.1)	0.47
Summer	1.10 (1-1.2)	0.04
Autumn	1.23 (1.1-1.4)	<0.001

The odds of confirming bovine TB lesions among the total lesions detected in summer (OR: 1.2, 95% CI:1.0-1.4, $p=0.14$) were higher when compared among the animals slaughtered in winter but the result was not statistically significant. The odds of confirming bovine TB lesions among the total lesions detected in autumn (OR: 1.2, 95% CI:1.0-1.5, $p<0.03$) were higher when compared among the animals slaughtered in winter and the result was statistically significant which is shown in Table 17.

Table 17: Univariable analysis for the association between the seasons of the animals slaughtered and risk of confirming bovine Tb lesions in Irish abattoirs during 2008.

Season	Odds Ratio (95% CI)	P-Value
Winter	Reference	-
spring	0.9 (0.8-1.2)	0.63
Summer	1.2 (1.0-1.4)	0.14
Autumn	1.2 (1.0-1.5)	0.03

Animal Origin:

With regards animal's origin (purchased or homebred), the odds of detecting suspected bovine TB lesions among purchased animals (OR: 1.3, 95% CI: 1.2-1.4, $p < 0.001$) were higher when compared with the homebred animals and the result was statistically significant as shown in Table 18.

Table 18: Univariable analysis for the association between the animal origin and risk of suspected bovine TB lesions detection among animals slaughtered in Irish abattoirs during 2008.

Animal Origin	Odds Ratio (95% CI)	P-Value
Home bred	Ref.	-
Purchased	1.3 (1.2-1.4)	<0.001

However, the odds of confirming the bovine TB lesion in purchased animals (OR: 1.0, 95% CI, 0.9-1.2, $p = 0.90$) were not significantly different than the odds of confirming bovine TB lesions in homebred animals (Table: 19).

Table 19: Univariable analysis for the association between the animal origin and risk of confirming bovine TB lesions in Irish abattoirs during 2008.

Animal Origin	Odds Ratio (95% CI)	P<0.05
Home bred	Reference	-
Purchased	1.0 (0.9-1.2)	0.90

Years Free:

The odds of detecting suspected bovine TB lesions were not significantly different with the increasing years free of bovine TB when compared to herds who were free for less than a year (Table 20).

Table 20: Univariable analysis for the association between the length of year free of herds from bovine TB and risk of suspected bovine TB lesions detections among animals slaughtered in Irish abattoirs during 2008.

Year Free	Odds Ratio (95% CI)	P Value
0-1	Reference	-
1-2	0.9 (0.8-1.1)	0.25
2-3	0.9 (0.8-1.0)	0.18
3-4	0.9 (0.8-1.0)	0.12
>4	0.8 (0.8-0.9)	<0.01

Similarly, the odds of confirming bovine TB among the lesions detected in Irish abattoirs with year free category were not significantly different (Table 21).

Table 21: Univariable analysis for the association between the length of year free of herds from bovine TB and risk of confirming bovine TB lesions in Irish abattoirs during 2008.

Year Free	Odds Ratio (95% CI)	P Value
0-1	Reference	-
1-2	1.1 (0.8-1.4)	0.70
2-3	1.0 (0.7-1.3)	0.91
3-4	0.7 (0.5-1.0)	0.06
>4	0.9 (0.7-1.0)	0.10

DED Risk Class:

The odds of detecting suspected bovine TB lesions were not significantly different from the increasing DED risk class “low” (OR: 1.0, 95% CI: 0.9-1.1, p=0.65) and “medium” (OR: 1.1, 95%CI: 1.0-1.2, p=0.08) when compared to risk class “very low”. However, the odds of

detecting suspected bovine TB lesions are higher in risk class “high” (OR: 1.4, 95%CI: 1.3-1.5, $p<0.001$) when compared to risk class “very low” and this difference was statistically significant, which is shown in Table 22.

Table 22: Univariable analysis for the association between the DED risk class and risk of suspected bovine TB lesion detections among animals slaughtered in Irish abattoirs during 2008.

DED Risk Class	Odds Ratio (95% CI)	P-Value
Very low	Ref	-
Low	1.0 (0.9-1.1)	0.65
Medium	1.1 (1-1.2)	0.08
High	1.4 (1.3-1.5)	<0.001

The odds of confirming bovine TB lesions were higher in risk class “medium” (OR: 1.4, 95% CI: 1.1-1.7, $p=0.002$) and “high” (OR: 1.8, 95% CI: 1.5-2, $p<0.001$) when compared to risk class “very low” and this difference was statistically significant which is illustrated in Table 23.

Table 23: Univariable analysis for the association between the DED risk class and risk of bovine TB lesion confirmations among animals slaughtered from attested herds in Irish abattoirs during 2008.

DED Risk Class	Odds Ratio (95% CI)	P-Value
Very low	Ref	-
Low	1.1 (0.9-1.4)	0.23
Medium	1.4 (1.1-1.7)	0.001
High	1.8 (1.5-2.1)	<0.001

3.3 Multivariable logistic regression analysis:

The adjusted OR for the detection of bovine TB lesions and the adjusted OR for confirmation of bovine TB lesions by each factor are described and listed below in Table 24.

Age:

The adjusted OR of detecting suspected bovine TB lesions increased with the increase in the age of animals and the results are statistically significant only among animal of ages greater than three years that is shown in Table 24. Similarly, the adjusted OR of confirming the suspected bovine TB lesions increased with the increase in the age of animals but they were not statistically significant which is shown in Table 24.

Gender:

The adjusted OR of detecting suspected bovine TB lesions was not higher among females (OR=0.9, 95% CI: 0.8-1.0) compared to male and the result was not statistically significant. The adjusted OR of confirming bovine TB lesions was higher among females (OR=1.4, 95% CI: 1.1-1.7) than males and the result was statistically significant as shown in Table 24.

Season:

The adjusted ORs detecting bovine TB lesions among the animals slaughtered in different seasons were different. The adjusted OR for the spring (OR=0.8, 95% CI: 0.8-0.9) is statistically significant but summer (OR=0.9, 95% CI: 0.8-1.0) and autumn (OR=1.0, 95% CI: 0.9-1.1) were not statistically different compared to winter (Table 24).

The adjusted OR of confirmation for spring (OR=0.9, 95% CI: 0.7-1.1), summer (OR=1.0, 95% CI: 0.8-1.3) and autumn (OR=1.2, 95% CI: 0.9-1.5) were not significantly different compared to winter shown in Table 24.

DED Risk Class:

The adjusted odds of detecting suspected bovine TB lesions were significantly higher in DED risk class of “high” (OR: 1.4, 95% CI: 1.2-1.5) in compared to risk class “very low”. The adjusted odds of confirming TB lesions were significantly higher in risk class “medium” (OR: 1.3, 95% CI:1.1-1.7) and “high” (OR: 1.7, 95% CI:1.4-2.2) when compared to risk class “very low” as shown in Table 24.

Years Free:

The adjusted odds of detecting suspected bovine TB lesions were not significantly different with herds free for more than four years of bovine TB (OR=1.0, 95% CI: 0.9-1.0) compared to herds who were free for less than a year (Table 24).

Herd Type:

The adjusted odds of detecting bovine TB lesions were significantly higher among suckler herd types (OR=1.1, 95% CI: 1.01-1.2) compared to beef herds. The odds of confirming bovine TB lesions were higher among suckler herds (OR=1.3, 95% CI: 1.1-1.6) compared to beef herds and the result is also statistically significant.

Animal Origin:

The adjusted odds of detecting bovine TB lesions were not significantly higher among the purchased animals (OR=1.1, 95% CI: 1.0-1.2) compared to home-bred. The adjusted odds of confirming bovine TB lesions were higher among the purchased animals (OR=1.2, 95% CI: 0.9-1.4) compared to homebred, but this difference was not statistically significant.

Table 24: Number of animals slaughtered for each confounding variables, the percentage of detection, percentage of confirmation and adjusted ORs of detection and confirmation.

Confounding factor	Class	Total number slaughtered	Total number detected	One or more lesions detected (%)	Submitted lesion confirmed (%)	Adjusted OR for	
						Detection (95% CI)	Confirmation (95%CI)
Age (years)	0-1	4,742	6	0.13	66.67	1.0 (reference)	1.0 (reference)
	1-2	332,673	518	0.16	58.12	1.2 (0.5 - 2.7)	1.0 (0.2-5.8)
	2-3	658,425	1,319	0.20	55.60	1.5 (0.7-3.4)	0.9 (0.2-5.6)
	3-4	107,067	382	0.36	56.54	2.5 (1.1-5.7)	1.0 (0.2-6.0)
	4-5	37,412	130	0.35	72.31	2.7 (1.2-6.3)	1.7 (0.3-10.9)
	5-6	31,047	115	0.37	70.43	2.9 (1.3-6.6)	1.6 (0.3-10.2)
	6-7	29,198	123	0.42	70.73	3.4 (1.5-7.7)	1.6 (0.3-10.3)
	7-8	28,419	123	0.43	81.30	3.5 (1.6-8.1)	3.0 (0.5-19.5)
	8-9	25,579	131	0.51	77.86	3.9 (1.7-9.1)	2.3 (0.4-14.9)
	9-10	22,952	118	0.51	75.42	3.9 (1.7-8.8)	1.7 (0.3-11.1)
	>10	84,681	472	0.56	80.30	4.2 (1.8-9.4)	2.2 (0.3-13.4)
Sex	Female	623,398	1,835	0.29	71.60	0.9 (0.8-1.01)	1.4 (1.1-1.7)
	Male	738,782	1,602	0.22	54.60	1.0 (reference)	1.0 (reference)
Season	Jan-Mar	329,340	771	0.23	61.50	1.0 (reference)	1.0 (reference)
	Apr-Jun	320,096	722	0.23	60.24	0.8 (0.8-0.9)	0.9 (0.7-1.1)
	Jul-Sep	364,747	943	0.26	64.90	0.9 (0.8-1.0)	1.0 (0.8-1.3)
	Oct-Dec	348,012	1,001	0.29	66.53	1.0 (0.9-1.1)	1.2 (0.9-1.5)
DED risk class	Very low	334,747	748	0.22	56.82	1.0 (reference)	1.0 (reference)
	Low	333,486	763	0.23	59.90	1.0 (0.9-1.1)	1.1 (0.9-1.4)
	Medium	337,129	824	0.24	64.81	1.1 (1.0-1.2)	1.3 (1.1-1.7)
	High	356,833	1,102	0.31	69.96	1.4 (1.2-1.5)	1.7 (1.4-2.2)
Year clear of TB	0-1	276,735	796	0.29	65.70	1.0 (reference)	1.0 (reference)
	1-2	147,476	395	0.27	66.83	1.0 (0.9-1.1)	1.0 (0.7-1.3)
	2-3	111,339	292	0.26	65.41	1.02 (0.9-1.2)	0.9 (0.7-1.3)
	3-4	80,431	205	0.25	58.54	1.0 (0.9-1.2)	0.7 (0.5-1.0)
	>4	720,867	1,715	0.24	62.22	1.0 (0.9-1.0)	0.9 (0.7-1.1)
Herd_type	Beef	420,855	1,066	0.25	57.32	1.0 (reference)	1.0 (reference)
	Dairy	359,627	639	0.18	59.78	0.7 (0.6-0.8)	0.9 (0.7-1.2)
	Others	22,168	68	0.31	61.76	0.8 (0.7-1.1)	1.0 (0.6-1.7)
Animal Origin	Sucklers	534,112	1,630	0.31	69.44	1.1 (1.01-1.2)	1.3 (1.1-1.6)
	Purchased	917,138	2,402	0.26	62.40	1.1 (1.0 -1.2)	1.23 (0.89-1.35)
	Home_bred	377,972	774	0.20	62.10	1.0 (reference)	1.0 (reference)

3.4 Adjusted ranking of abattoirs (slaughterhouses):

The abattoirs were ranked from 1 to 31 (1 being the best and 31 being the worst abattoir) after adjusting bovine TB detection risks by animal/herd characteristics known to be associated with bovine TB in Ireland (Table 25). Similarly, abattoirs were ranked from 1 to 30 (1 being the best factory and 30 being the worst) after adjusting confirmation risks by animal/herd characteristics known to affect the probability of confirming bovine TB lesions in Ireland (Table 26).

Table 25: The crude and adjusted risk of bovine TB lesions detection, and abattoir ranking (high to low), in Ireland during 2008.

All animals from attested herds				Animals from attested herd with complete data on confounding factors				
Abattoir No	Number Slaughtered	Crude Risk (%)	Crude Rank	Number Slaughtered	Adjusted Risk (%)	Adjusted Rank	Crude Risk (%)	Crude Rank
1	72,238	0.25	11	64,521	0.32	14	0.26	12
2	53,409	0.17	24	51,874	0.23	21	0.17	23
3	60,007	0.23	17	59,166	0.29	17	0.22	17
4	78,932	0.11	30	75,797	0.14	29	0.10	30
5	57,711	0.33	6	50,273	0.44	6	0.33	6
6	57,555	0.14	26	55,972	0.2	25	0.14	26
7	53,278	0.3	9	50,874	0.39	8	0.30	8
8	59,533	0.12	27	56,820	0.15	27	0.11	28
9	58,179	0.3	8	56,896	0.42	7	0.30	7
10	72,194	0.53	2	60,557	0.62	1	0.56	1
11	46,334	0.2	20	45,276	0.28	18	0.20	20
12	54,986	0.23	16	52,689	0.33	11	0.23	16
13	2,438	0.25	14	2,381	0.32	12	0.25	14
14	39,041	0.24	15	37,084	0.31	15	0.23	15
15	52,528	0.19	21	49,346	0.24	20	0.18	22
16	54,117	0.17	25	51,576	0.23	23	0.17	24
17	71,482	0.56	1	66,580	0.61	2	0.52	2
18	4,766	0.21	19	4,746	0.23	22	0.21	18
19	52,210	0.3	7	46,765	0.36	9	0.27	10
20	50,015	0.43	4	47,617	0.53	4	0.41	4
21	9,772	0.08	31	9,065	0.1	31	0.08	31
22	39,612	0.12	28	39,233	0.12	30	0.12	27
23	58	0.00	33	-	-	-	-	-
24	47,408	0.00	32	-	-	-	-	-
25	50,292	0.18	22	48,766	0.22	24	0.16	25
26	27,935	0.40	5	26,349	0.5	5	0.40	5
27	22,263	0.28	10	20,717	0.35	10	0.28	9
28	39,233	0.52	3	38,051	0.61	3	0.52	3
29	17,617	0.21	18	16,856	0.3	16	0.21	19
30	50,015	0.18	23	1,078	0.2	26	0.19	21
31	667	0	33	-	-	-	-	-
32	41,456	0	33	-	-	-	-	-
33	5,399	0.11	29	5,297	0.14	28	0.11	29
34	3155	0.25	12	3,138	0.27	19	0.25	13
35	5267	0.25	13	4,892	0.32	13	0.27	11
Total	1,362,195			1,200,252				
Average		0.25			0.32		0.25	

Table 26: The crude and adjusted risk of bovine TB lesions confirmation, and abattoir ranking (high to low), in Ireland during 2008.

All animals from the attested herds				Animals from attested herd with complete data on confounding factors				
Abattoir No	Number Detected	Crude Risk (%)	Crude Rank	Number Detected	Adjusted Risk (%)	Adjusted Rank	Crude Risk (%)	Crude Rank
1	184	63.6	16	166	62	17	63.6	15
2	91	86.8	3	89	87	2	86.8	2
3	137	54.0	26	133	53	23	54.0	25
4	84	86.9	2	76	88	1	86.9	1
5	189	54.5	25	167	53	24	54.5	24
6	80	66.3	13	79	67	9	66.3	12
7	158	65.2	15	153	65	13	65.2	14
8	72	81.9	4	65	82	3	81.9	3
9	176	60.2	20	172	60	18	60.2	19
10	383	66.8	10	342	66	12	66.8	9
11	93	55.9	24	89	55	22	55.9	23
12	129	57.4	22	122	55	21	57.4	21
13	6	66.7	11	6	67	10	66.7	10
14	94	62.8	18	86	62	16	62.8	17
15	100	57.0	23	88	52	25	57.0	22
16	90	60.0	21	86	60	19	60.0	20
17	397	66.3	14	345	65	14	66.3	12
18	10	30.0	30	10	30	29	30.0	29
19	158	69.0	9	128	68	8	69.0	8
20	216	70.4	8	194	68	7	70.4	7
21	8	62.5	19	7	57	20	62.5	18
22	47	76.6	5	47	77	4	76.6	4
23	0	0.0	32	-	-	-	-	-
24	1	100.0	1	-	-	-	-	-
25	91	75.8	6	80	73	5	75.8	5
26	111	63.1	17	105	64	15	63.1	16
27	63	71.4	7	59	72	6	71.4	6
28	203	40.9	28	196	42	27	40.9	27
29	37	48.7	27	35	51	26	48.7	26
30	2	0.0	32	-	-	-	-	-
31	0	0.0	32	-	-	-	-	-
32	0	0.0	32	-	-	-	-	-
33	6	66.7	11	6	67	10	66.7	10
34	8	25.0	31	8	25	25	25.0	30
35	13	30.8	29	13	30	30	30.8	28
Total	3,437			3,152				
Average		62.7			61		61.4	

CHAPTER 4: DISCUSSION

Bovine TB surveillance in Ireland mainly consists of two components: skin testing (SICCT) and slaughter surveillance. The main aim of this study was to compare the effectiveness of abattoirs in detecting suspected bovine TB lesions and their subsequent confirmation from cattle classified as negative for bovine TB based on skin test results.

The crude detection risk of the suspected bovine TB lesions among the abattoirs ranges from 0 to 56 per 10,000 animals slaughtered (Table 25) with an average of 25 per 10,000 animals slaughtered. Similar results (ranged from 0 to 58 per 10,000 animals slaughtered with average of 22 per 10,000 animals slaughtered) were shown by Frankena et al. (2005) and (ranged from 0 to 52 per 10,000 animals slaughtered and average of 25 per 10,000 animals slaughtered) Olea-Popelka et al. (2012). After exclusion of nine abattoirs that detected less than 10 suspected bovine TB lesions, the crude bovine TB detection risk ranged from 11 to 58 per 10,000 animals slaughtered (a five-fold difference between abattoirs), which was identical to the results obtained by Olea-Popelka et al. (2012), but lower than a similar study by Frankena et al. (2007) and Martin et al. (2003), who found a sevenfold difference after controlling for year, month and animal type.

On the other hand, the crude confirmation risk for bovine TB lesions among the suspected bovine TB lesions ranged from 0 to 100 % with an average of 62.7% as shown in Table 26. This result is similar to the study by Frankena et al. (2007) who found an average crude confirmation risk of 63% but slightly lower than the study by Olea-Popelka et al. (2012) who found the crude

confirmation risk to be 67.5%. After excluding the abattoirs that submitted less than 10 lesions, the crude confirmation risks ranged from 41 to 87% (two-fold difference between the abattoirs).

Thus, this study shows that there is wide variation in the risks of detection of bovine TB lesions among Irish abattoirs. Variation in bovine TB lesion detection has been mentioned in other studies and attributed to physical settings (e.g. abattoir line speed, light) and the inspector's efficiencies in abattoirs (Corner, 1994; Frankena et al., 2007; Olea-Popelka et al., 2012; Pascual-Linaza et al., 2016). Improvements should be done in those abattoirs where the detection risk was low. Intervention measures should be applied to increase the ability of abattoirs in detecting the bovine TB lesions during the slaughter (Pascual-Linaza et al., 2016).

After adjusting our results by all factors included in this analysis, our multivariable results indicated that bovine TB lesions were more likely to be found in older animals. There were statistically significant differences in detecting suspected bovine TB lesions among animals greater three years of age when compared to animals younger than a year old in this study. This can be explained because bovine TB is a chronic disease in nature and the longer the animals live, the higher the chance of developing bovine TB lesions, and thus, be found during slaughter. This result was in agreement with the earlier studies by Frankena et al. (2007), Olea-Popelka et al. (2012) conducted in Ireland and with the study by Pascual-Linaza et al. (2016) in Northern Ireland.

Bovine TB lesions were more likely to be detected at the abattoir and confirmed in the laboratory among animals from suckler herds. The results were consistent with the conclusion drawn by

study of Clegg et al. (2016). According to Clegg et al. (2016), animals in suckler herds go out in the pasture to graze with their calves and they were in contact with their mothers for much longer periods than dairy calves. This would provide greater opportunity for transmission.

Bovine TB lesions were more likely to be detected and confirmed from animals slaughtered during summer (Jul-Sep) and autumn (Oct-Dec) than winter, but the results were not significantly higher during these seasons after the multivariable analysis. The result is slightly different from the conclusion drawn by Frankena et al. (2007) who found that the odds of detecting bovine TB lesion was higher in animals that are slaughtered in winter months. Bovine TB Lesions were more likely to be detected and confirmed from animals that came from the areas (DED in Ireland) with higher animal prevalence. Thus, animals from DED risks categories “medium” and “high” were more likely to be detected for TB lesions compared to DED risks category “very low”, because former DED risks categories have higher animal level disease prevalence.

Purchased animals were more likely to have suspected bovine TB lesions at the slaughter house compared to home bred animals, but this difference was not statistically significant. This result was almost similar to the study by Frankena et al. (2007) and the Olea-Popelka et al. (2012) in same Irish slaughter houses. The same information was drawn in a similar study done in Northern Ireland by Pascual-Linaza et al. (2016).

With the increasing years free of TB, the slaughtered animals were less likely to have lesions detected compared to the animals who were free for less than a year but the results are not

statistically significant (Table 20). The results obtained by this study were similar to the study by Frankena et al. (2007) who did a study in similar Irish settings.

In general, the abattoir ranking, after adjusting for all potential confounding factors, was not affected considerably by these animal and herd level factors; thus, indicating that these factors did not substantially contribute to the variation in the risk of bovine TB lesion detection nor lesion confirmation among abattoirs.

The postmortem examination procedure to detect lesions is not 100% sensitive (Corner, 1994), who had mentioned 47% of the lesions were detected in abattoir examination in his study. Similarly, a study conducted in Spain by Garcia-Saenz et al. (2015) had estimated the median sensitivity of 31.4% (95% CI: 28.6 to 36.2%) and a report compiled by the European Food Safety Authority (EFSA) Panel on Animal Health and Welfare (AHAW), (2012), reported a mean sensitivity of 71% (95% CI: 38 to 92%) from six different studies.

Inspectors were not able to identify bovine TB lesions that were not visible to their eye. Bovine TB lesions at the incipient stage may be located mostly at lower parts of the respiratory tract that needs careful dissection and examinations (Domingo et al., 2014; Kantor, et al., 1987). Also, not all the infected animals have lesions present during the time of slaughter. Besides, the interplay of the host defense mechanisms and the virulence factors of mycobacteria also play the role in formation of visible lesions in infected animals (Domingo et al., 2014).

There was a wide variation in the confirmation risk among the abattoirs (Frankena et al., 2007).

The reasons for the wide variations in the confirmations risk was due to the variation in the efficiencies of lesions detection at individual slaughter house (Frankena et al., 2007; Olea-Popelka et al., 2012). For example, it was difficult to differentiate the suspected bovine TB lesions from the non-tuberculous granulomas caused by actinomycosis ('lumpy jaw'), actinobacillosis ('wooden tongue'), paratuberculosis ('Johne's disease'), neoplasms and other lesions based on visual inspection of a carcass (Ritacco et al., 2006, Frankena et al., 2007).

Although the SICCT is the primary method of screening TB in Ireland, slaughter surveillance is a complementary and important method for detecting bovine TB lesions at the abattoir (Frankena et al., 2007). Animals may be non-reactive to tuberculin but the lesions can be identified at slaughter. The sensitivity and effectiveness of bovine TB slaughter surveillance needs to be monitored to identify those factors that impact the effectiveness of finding bovine TB lesions at the abattoir. This study underscores the fact that there was a variation in effectiveness of abattoirs in surveillance of bovine TB in Ireland; yet, still there is a room of improvement. Bovine TB slaughter surveillance need to be constantly monitored to evaluate its effectiveness and to improve factors affecting it (e.g. physical facilities and personnel) in order to maximize the detection of infected animals and herds. Strengthening the slaughter surveillance is one of the key component in achieving the national plan of bovine TB control and eradication in Ireland.

CHAPTER 5: CONCLUSION

This study shows the importance of slaughter surveillance program in Republic of Ireland. There has been a progress in bovine TB lesions detections among Irish abattoirs compared to the previous studies (2007 and 2012). Still, this study shows that there is an opportunity to explore strategies to further improve the overall effectiveness of abattoirs surveillance for bovine TB. Improvements of the physical settings and human components of abattoirs surveillance are necessary to increase effectiveness of bovine TB lesions detection among abattoirs with lower rankings. Finally, a continuous monitoring process is required among Irish abattoirs to maximize the effectiveness of bovine TB lesions detection during slaughter surveillance.

REFERENCES

- Abernethy, D. A., Upton, P., Higgins, I. M., McGrath, G., Goodchild, A. V., Rolfe, S. J., ...
More, S. J. (2013). Bovine tuberculosis trends in the UK and the Republic of Ireland,
1995–2010. *Veterinary Record*, 172(12), 312–312. <https://doi.org/10.1136/vr.100969>
- Alvarez, J., Perez, A. M., Bezos, J., Casal, C., Romero, B., Rodriguez-Campos, S., ...
Domínguez, L. (2012). Eradication of bovine tuberculosis at a herd-level in Madrid,
Spain: study of within-herd transmission dynamics over a 12 year period. *BMC
Veterinary Research*, 8(1), 100. <https://doi.org/10.1186/1746-6148-8-100>
- Amanfu, W. (2006). The situation of tuberculosis and tuberculosis control in animals of
economic interest. *Tuberculosis*, 86(3–4), 330–335.
<https://doi.org/10.1016/j.tube.2006.01.007>
- Arentz, M., & Hawn, T. R. (2007). Tuberculosis infection: Insight from immunogenomics. *Drug
Discovery Today: Disease Mechanisms*, 4(4), 231–236.
<https://doi.org/10.1016/j.ddmec.2007.11.003>
- Asseged, B., Woldeesenbet, Z., Yimer, E., & Lemma, E. (2004). Evaluation of Abattoir
Inspection for the Diagnosis of Mycobacterium bovis Infection in Cattle at Addis Ababa
Abattoir. *Tropical Animal Health and Production*, 36(6), 537–546.
<https://doi.org/10.1023/B:TROP.0000040934.32330.44>
- Ayele, W. Y., Neill, S. D., Zinsstag, J., Weiss, M. G., & Pavlik, I. (2004). Bovine tuberculosis:
an old disease but a new threat to Africa. *The International Journal of Tuberculosis and
Lung Disease*, 8(8), 924–937.

- Aznar, I., McGrath, G., Murphy, D., Corner, L. A. L., Gormley, E., Frankena, K., ... De Jong, M. C. M. (2011). Trial design to estimate the effect of vaccination on tuberculosis incidence in badgers. *Veterinary Microbiology*, *151*(1–2), 104–111.
<https://doi.org/10.1016/j.vetmic.2011.02.032>
- Berrian, A. M., O’Keeffe, J., White, P. W., Norris, J., Litt, J., More, S. J., & Olea-Popelka, F. J. (2012). Risk of bovine tuberculosis for cattle sold out from herds during 2005 in Ireland. *Veterinary Record*, *170*(24), 620–620. <https://doi.org/10.1136/vr.100674>
- Byrne, A. W., Kenny, K., Fogarty, U., O’Keeffe, J. J., More, S. J., McGrath, G., ... Dohoo, I. R. (2015). Spatial and temporal analyses of metrics of tuberculosis infection in badgers (*Meles meles*) from the Republic of Ireland: Trends in apparent prevalence. *Preventive Veterinary Medicine*, *122*(3), 345–354. <https://doi.org/10.1016/j.prevetmed.2015.10.013>
- Christensen, J., & Gardner, I. A. (2000). Herd-level interpretation of test results for epidemiologic studies of animal diseases. *Preventive Veterinary Medicine*, *45*(1–2), 83–106. [https://doi.org/10.1016/S0167-5877\(00\)00118-5](https://doi.org/10.1016/S0167-5877(00)00118-5)
- Clegg, T. A., Blake, M., Healy, R., Good, M., Higgins, I. M., & More, S. J. (2013). The impact of animal introductions during herd restrictions on future herd-level bovine tuberculosis risk. *Preventive Veterinary Medicine*, *109*(3–4), 246–257.
<https://doi.org/10.1016/j.prevetmed.2012.10.005>
- Clegg, T. A., Good, M., & More, S. J. (2016). Risk factors for cattle presenting with a confirmed bTB lesion at slaughter, from herds with no evidence of within-herd transmission. *Preventive Veterinary Medicine*, *126*, 111–120.
<https://doi.org/10.1016/j.prevetmed.2016.02.003>

- Clegg, T. A., More, S. J., Higgins, I. M., Good, M., Blake, M., & Williams, D. H. (2008). Potential infection-control benefit for Ireland from pre-movement testing of cattle for tuberculosis. *Preventive Veterinary Medicine*, 84(1–2), 94–111.
<https://doi.org/10.1016/j.prevetmed.2007.11.004>
- Collins, J. D. (2006). Tuberculosis in cattle: Strategic planning for the future. *Veterinary Microbiology*, 112(2–4), 369–381. <https://doi.org/10.1016/j.vetmic.2005.11.041>
- Corner, L. A. (1994). Post mortem diagnosis of *Mycobacterium bovis* infection in cattle. *Veterinary Microbiology*, 40(1–2), 53–63. [https://doi.org/10.1016/0378-1135\(94\)90046-9](https://doi.org/10.1016/0378-1135(94)90046-9)
- Corner, L. A. L., Murphy, D., & Gormley, E. (2011). *Mycobacterium bovis* Infection in the Eurasian Badger (*Meles meles*): the Disease, Pathogenesis, Epidemiology and Control. *Journal of Comparative Pathology*, 144(1), 1–24.
<https://doi.org/10.1016/j.jcpa.2010.10.003>
- Corner, L. A. L., O’Meara, D., Costello, E., Lesellier, S., & Gormley, E. (2012). The distribution of *Mycobacterium bovis* infection in naturally infected badgers. *The Veterinary Journal*, 194(2), 166–172. <https://doi.org/10.1016/j.tvjl.2012.03.013>
- Cosivi, O., Grange, J. M., Daborn, C. J., Raviglione, M. C., Fujikura, T., Cousins, D., ... Meslin, F. X. (1998). Zoonotic tuberculosis due to *Mycobacterium bovis* in developing countries. *Emerging Infectious Diseases*, 4(1), 59.
- de la Rua-Domenech, R., Goodchild, A. T., Vordermeier, H. M., Hewinson, R. G., Christiansen, K. H., & Clifton-Hadley, R. S. (2006). Ante mortem diagnosis of tuberculosis in cattle: A review of the tuberculin tests, γ -interferon assay and other ancillary diagnostic techniques. *Research in Veterinary Science*, 81(2), 190–210.
<https://doi.org/10.1016/j.rvsc.2005.11.005>

- Domingo, M., Vidal, E., & Marco, A. (2014). Pathology of bovine tuberculosis. *Research in Veterinary Science*, 97, S20–S29. <https://doi.org/10.1016/j.rvsc.2014.03.017>
- Doran, P., Carson, J., Costello, E., & More, S. J. (2009). An outbreak of tuberculosis affecting cattle and people on an Irish dairy farm, following the consumption of raw milk. *Irish Veterinary Journal*, 62(6), 390.
- Drewe, J. A., O'Connor, H. M., Weber, N., McDONALD, R. A., & Delahay, R. J. (2013). Patterns of direct and indirect contact between cattle and badgers naturally infected with tuberculosis. *Epidemiology and Infection*, 141(7), 1467–1475. <https://doi.org/10.1017/S0950268813000691>
- Drewe, J. A., Pfeiffer, D. U., & Kaneene, J. B. (2014). Epidemiology of *Mycobacterium bovis*. In C. O. Thoen, J. H. Steele, & J. B. Kaneene (Eds.), *Zoonotic Tuberculosis* (pp. 63–77). Chichester, UK: John Wiley & Sons, Inc. Retrieved from <http://doi.wiley.com/10.1002/9781118474310.ch6>
- Duignan, A., Good, M., & More, S. J. (2012). Quality control in the national bovine tuberculosis eradication programme in Ireland. *Rev. Sci. Tech*, 31, 845–860.
- EFSA Panel on Animal Health and Welfare (AHAW). (2012). Scientific Opinion on the use of a gamma interferon test for the diagnosis of bovine tuberculosis: bovine TB Test. *EFSA Journal*, 10(12), 2975. <https://doi.org/10.2903/j.efsa.2012.2975>
- Egbe, N. F., Muwonge, A., Ndip, L., Kelly, R. F., Sander, M., Tanya, V., ... Bronsvoort, B. M. de C. (2016). Abattoir-based estimates of mycobacterial infections in Cameroon. *Scientific Reports*, 6, 24320. <https://doi.org/10.1038/srep24320>

- European Food Safety Authority (Ed.). (2009). *Trends and sources of zoonoses and zoonotic agents in the European Union in 2007; the Community summary report 1* (20 January 2009). Parma: EFSA.
- Frankena, K., White, P. W., O'keeffe, J., Costello, E., Martin, S. W., Van Grevenhof, I., & More, S. J. (2007). Quantification of the relative efficiency of factory surveillance in the disclosure of tuberculosis lesions in attested Irish cattle. *Veterinary Record: Journal of the British Veterinary Association*, 161(20).
- Gallagher, M. J., Higgins, I. M., Clegg, T. A., Williams, D. H., & More, S. J. (2013). Comparison of bovine tuberculosis recurrence in Irish herds between 1998 and 2008. *Preventive Veterinary Medicine*, 111(3–4), 237–244.
<https://doi.org/10.1016/j.prevetmed.2013.05.004>
- Garcia-Saenz, A., Napp, S., Lopez, S., Casal, J., & Allepuz, A. (2015). Estimation of the individual slaughterhouse surveillance sensitivity for bovine tuberculosis in Catalonia (North-Eastern Spain). *Preventive Veterinary Medicine*, 121(3–4), 332–337.
<https://doi.org/10.1016/j.prevetmed.2015.08.008>
- Good, M. (2006). Bovine tuberculosis eradication in Ireland. *Irish Veterinary Journal*, 59(3), 154.
- Good, M., Clegg, T. A., Duignan, A., & More, S. J. (2011). Impact of the national full herd depopulation policy on the recurrence of bovine tuberculosis in Irish herds, 2003 to 2005. *Veterinary Record*, 169(22), 581–581. <https://doi.org/10.1136/vr.d4571>
- Goodchild, A. V., & Clifton-Hadley, R. S. (2001). Cattle-to-cattle transmission of *Mycobacterium bovis*. *Tuberculosis*, 81(1–2), 23–41.
<https://doi.org/10.1054/tube.2000.0256>

- Goodchild, A. V., Downs, S. H., Upton, P., Wood, J. L. N., & de la Rua-Domenech, R. (2015). Specificity of the comparative skin test for bovine tuberculosis in Great Britain. *Veterinary Record*, 177(10), 258–258. <https://doi.org/10.1136/vr.102961>
- Green, L. E., & Cornell, S. J. (2005). Investigations of cattle herd breakdowns with bovine tuberculosis in four counties of England and Wales using VETNET data. *Preventive Veterinary Medicine*, 70(3–4), 293–311. <https://doi.org/10.1016/j.prevetmed.2005.05.005>
- Griffin, J. M., Williams, D. H., Kelly, G. E., Clegg, T. A., O’Boyle, I., Collins, J. D., & More, S. J. (2005). The impact of badger removal on the control of tuberculosis in cattle herds in Ireland. *Preventive Veterinary Medicine*, 67(4), 237–266. <https://doi.org/10.1016/j.prevetmed.2004.10.009>
- Humblet, M.-F., Boschioli, M. L., & Saegerman, C. (2009). Classification of worldwide bovine tuberculosis risk factors in cattle: a stratified approach. *Veterinary Research*, 40(5), 50. <https://doi.org/10.1051/vetres/2009033>
- Humphrey, H. M., Orloski, K. A., & Olea-Popelka, F. J. (2014). Bovine tuberculosis slaughter surveillance in the United States 2001–2010: assessment of its traceback investigation function. *BMC Veterinary Research*, 10(1), 1.
- Hunter, D. L. (1996). Tuberculosis in free-ranging, semi free-ranging and captive cervids. *Revue Scientifique Et Technique (International Office of Epizootics)*, 15(1), 171–181.
- Inwald, J., Hinds, J., Palmer, S., Dale, J., Butcher, P. D., Hewinson, R. G., & Gordon, S. V. (2003). Genomic Analysis of Mycobacterium tuberculosis Complex Strains Used for Production of Purified Protein Derivative. *Journal of Clinical Microbiology*, 41(8), 3929–3932. <https://doi.org/10.1128/JCM.41.8.3929-3932.2003>

- Kaneene, J. B., Miller, R., & Meyer, R. M. (2006). Abattoir surveillance: The U.S. experience. *Veterinary Microbiology*, 112(2–4), 273–282.
<https://doi.org/10.1016/j.vetmic.2005.11.018>
- Kantor, I. N. de, Nader, A., Bernardelli, A., Girón, D. O., & Man, E. (1987). Tuberculous infection in cattle not detected by slaughterhouse inspection. *Journal of Veterinary Medicine, Series B*, 34(1–10), 202–205.
- Lahuerta-Marin, A., McNair, J., Skuce, R., McBride, S., Allen, M., Strain, S. A. J., ... Byrne, A. W. (2016). Risk factors for failure to detect bovine tuberculosis in cattle from infected herds across Northern Ireland (2004–2010). *Research in Veterinary Science*, 107, 233–239. <https://doi.org/10.1016/j.rvsc.2016.06.014>
- Menin, Á., Fleith, R., Reck, C., Marlow, M., Fernandes, P., Pilati, C., & Báfica, A. (2013). Asymptomatic Cattle Naturally Infected with *Mycobacterium bovis* Present Exacerbated Tissue Pathology and Bacterial Dissemination. *PLoS ONE*, 8(1), e53884.
<https://doi.org/10.1371/journal.pone.0053884>
- Michel, A. L. (2002). Implications of tuberculosis in African wildlife and livestock. *Annals of the New York Academy of Sciences*, 969, 251–255.
- Michel, A. L., Müller, B., & van Helden, P. D. (2010). *Mycobacterium bovis* at the animal–human interface: A problem, or not? *Veterinary Microbiology*, 140(3–4), 371–381.
<https://doi.org/10.1016/j.vetmic.2009.08.029>
- Monaghan, M. L., Doherty, M. L., Collins, J. D., Kazda, J. F., & Quinn, P. J. (1994). The tuberculin test. *Veterinary Microbiology*, 40(1), 111–124.
[https://doi.org/http://dx.doi.org/10.1016/0378-1135\(94\)90050-7](https://doi.org/http://dx.doi.org/10.1016/0378-1135(94)90050-7)

- More, S., Collins, D. M., University College, D., School of Agriculture, F. S. & V. M., Centre for Veterinary Epidemiology and Risk Analysis, University College, D., ... Badger Vaccine Project. (2010). *Biennial Report, 2008-09*. Dublin: The Centre for Veterinary Epidemiology and Risk Analysis, The TB Diagnostics and Immunology Research Centre, The Badger Vaccine Project.
- More, S. J., & Good, M. (2015). Understanding and managing bTB risk: Perspectives from Ireland. *Veterinary Microbiology*, 176(3–4), 209–218.
<https://doi.org/10.1016/j.vetmic.2015.01.026>
- Morrison, W. I., Bourne, F. J., Cox, D. R., Donnelly, C. A., Gettinby, G., McInerney, J. P., & Woodroffe, R. (2000). Pathogenesis and diagnosis of infections with *Mycobacterium bovis* in cattle. Independent Scientific Group on Cattle TB. *The Veterinary Record*, 146(9), 236–242.
- Müller, B., Dürr, S., Alonso, S., Hattendorf, J., Laisse, C. J. M., Parsons, S. D. C., ... Zinsstag, J. (2013). Zoonotic *Mycobacterium bovis* –induced Tuberculosis in Humans. *Emerging Infectious Diseases*, 19(6), 899–908. <https://doi.org/10.3201/eid1906.120543>
- Murphy, D., Gormley, E., Costello, E., O’Meara, D., & Corner, L. A. L. (2010). The prevalence and distribution of *Mycobacterium bovis* infection in European badgers (*Meles meles*) as determined by enhanced post mortem examination and bacteriological culture. *Research in Veterinary Science*, 88(1), 1–5. <https://doi.org/10.1016/j.rvsc.2009.05.020>
- O’Garra, A., Redford, P. S., McNab, F. W., Bloom, C. I., Wilkinson, R. J., & Berry, M. P. R. (2013). The Immune Response in Tuberculosis. *Annual Review of Immunology*, 31(1), 475–527. <https://doi.org/10.1146/annurev-immunol-032712-095939>

- Olea-Popelka, F., Freeman, Z., White, P., Costello, E., O’Keeffe, J., Frankena, K., ... More, S. (2012). Relative effectiveness of Irish factories in the surveillance of slaughtered cattle for visible lesions of tuberculosis, 2005-2007. *Irish Veterinary Journal*, 65(1), 1.
- Olea-Popelka, F. J., Costello, E., White, P., McGrath, G., Collins, J. D., O’Keeffe, J., ... Martin, S. W. (2008). Risk factors for disclosure of additional tuberculous cattle in attested-clear herds that had one animal with a confirmed lesion of tuberculosis at slaughter during 2003 in Ireland. *Preventive Veterinary Medicine*, 85(1–2), 81–91.
<https://doi.org/10.1016/j.prevetmed.2008.01.003>
- Olea-Popelka, F. J., Flynn, O., Costello, E., McGrath, G., Collins, J. D., O’Keeffe, J., ... Martin, S. W. (2005). Spatial relationship between *Mycobacterium bovis* strains in cattle and badgers in four areas in Ireland. *Preventive Veterinary Medicine*, 71(1–2), 57–70.
<https://doi.org/10.1016/j.prevetmed.2005.05.008>
- Olea-Popelka, F. J., White, P. W., Collins, J. D., O’Keeffe, J., Kelton, D. F., & Martin, S. W. (2004). Breakdown severity during a bovine tuberculosis episode as a predictor of future herd breakdowns in Ireland. *Preventive Veterinary Medicine*, 63(3–4), 163–172.
<https://doi.org/10.1016/j.prevetmed.2004.03.001>
- Olea-Popelka, F., Muwonge, A., Perera, A., Dean, A. S., Mumford, E., Erlacher-Vindel, E., ... Fujiwara, P. I. (2017). Zoonotic tuberculosis in human beings caused by *Mycobacterium bovis* —a call for action. *The Lancet Infectious Diseases*, 17(1), e21–e25.
[https://doi.org/10.1016/S1473-3099\(16\)30139-6](https://doi.org/10.1016/S1473-3099(16)30139-6)
- Pascual-Linaza, A. V., Gordon, A. W., Stringer, L. A., & Menzies, F. D. (2016). Efficiency of slaughterhouse surveillance for the detection of bovine tuberculosis in cattle in Northern Ireland. *Epidemiology and Infection*, 1–11. <https://doi.org/10.1017/S0950268816003095>

- Pérez-Lago, L., Navarro, Y., & García-de-Viedma, D. (2014). Current knowledge and pending challenges in zoonosis caused by *Mycobacterium bovis*: A review. *Research in Veterinary Science*, 97, S94–S100. <https://doi.org/10.1016/j.rvsc.2013.11.008>
- Pollock, J. M., & Neill, S. D. (2002). *Mycobacterium bovis* infection and tuberculosis in cattle. *Veterinary Journal (London, England: 1997)*, 163(2), 115–127.
- Pollock, J. M., Rodgers, J. D., Welsh, M. D., & McNair, J. (2006). Pathogenesis of bovine tuberculosis: The role of experimental models of infection. *Veterinary Microbiology*, 112(2–4), 141–150. <https://doi.org/10.1016/j.vetmic.2005.11.032>
- Rogers, L., Delahay, R., Hounscome, T., & Cheeseman, C. (2000). Changes in badger, *Meles meles*, social organisation in response to increasing population density at Woodchester Park, south-west England. *Mustelids in the Modern World. Management and Conservation Aspects of Small Carnivore: Human Interactions*, 267–279.
- Schiller, I., RayWaters, W., Vordermeier, H. M., Jemmi, T., Welsh, M., Keck, N., ... Oesch, B. (2011). Bovine tuberculosis in Europe from the perspective of an officially tuberculosis free country: Trade, surveillance and diagnostics. *Veterinary Microbiology*, 151(1–2), 153–159. <https://doi.org/10.1016/j.vetmic.2011.02.039>
- Sheridan, M. (2011). Progress in tuberculosis eradication in Ireland. *Veterinary Microbiology*, 151(1–2), 160–169. <https://doi.org/10.1016/j.vetmic.2011.02.040>
- Shittu, A., Clifton-Hadley, R. S., Ely, E. R., Upton, P. U., & Downs, S. H. (2013). Factors associated with bovine tuberculosis confirmation rates in suspect lesions found in cattle at routine slaughter in Great Britain, 2003–2008. *Preventive Veterinary Medicine*, 110(3–4), 395–404. <https://doi.org/http://dx.doi.org/10.1016/j.prevetmed.2013.03.001>

- Thoen, C. O., LoBue, P. A., & de Kantor, I. (2010). Why has zoonotic tuberculosis not received much attention [Editorial]. *The International Journal of Tuberculosis and Lung Disease*, 14(9), 1073–1074.
- Wangoo, A., Johnson, L., Gough, J., Ackbar, R., Inglut, S., Hicks, D., ... Vordermeier, M. (2005). Advanced granulomatous lesions in *Mycobacterium bovis*-infected cattle are associated with increased expression of type I procollagen, gammadelta (WC1+) T cells and CD 68+ cells. *Journal of Comparative Pathology*, 133(4), 223–234.
<https://doi.org/10.1016/j.jcpa.2005.05.001>
- Winkler, B., & Mathews, F. (2015). Environmental risk factors associated with bovine tuberculosis among cattle in high-risk areas. *Biology Letters*, 11(11), 20150536.
<https://doi.org/10.1098/rsbl.2015.0536>
- Wolfe, D. M., Berke, O., More, S. J., Kelton, D. F., White, P. W., O’Keeffe, J. J., & Martin, S. W. (2009). The risk of a positive test for bovine tuberculosis in cattle purchased from herds with and without a recent history of bovine tuberculosis in Ireland. *Preventive Veterinary Medicine*, 92(1–2), 99–105. <https://doi.org/10.1016/j.prevetmed.2009.07.012>